American Journal of Diseases of Children

Vol. 6 AUGUST, 1913 No. 2

PANCREATIC INSUFFICIENCY *

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A severe indigestion of acute onset and protracted course, characterized by the evacuation of bulky, pale-gray, greasy stools, occurs fairly often in early childhood. Marked wasting is a feature, as is the occurrence of periods of amelioration during the earlier months of the affection. The stools invariably contain a large amount of wasted fat which is excreted unsplit, and in the graver examples of the disease starches are passed undigested, and sometimes proteins even escape digestive action.

English writers have called this symptom group "Coeliac disease." Robert Hutchison has written a lucid clinical description of it, and in his paper he quotes opinions of Cheadle, Gee and Gibbons on the subject. Eustace Smith has also considered this symptom-complex at length in his lectures on "The Wasting Diseases of Children." The English writers seem inclined to attribute the fat waste to an unexplained diminution in the fat-absorbing powers of the celiac lymphatic system.

In America, Herter, searching for a type of possible onset for those cases of infantilism which he believed to be of intestinal origin, made a study of such cases which he describes as acute and subacute intestinal affections leading to infantilism. His account is worthy of reproduction:

HERTER'S INFANTILISM

Such cases begin, for the most part, between the end of the first and the middle of the third year; they are characterized by diarrhea, usually without tenesmus, with an abundance of mucus but no blood. The diarrheal discharges are usually not frequent, while the loss of weight is not rapid — about one-half ounce daily — it may progress until the child is much emaciated. There is usually considerable flatulence. There is a moderate or marked fall in hemoglobin; the temperature is normal, or subnormal, the appetite is unimpaired. The disease lasts from three to six weeks and recurrences are very apt to occur. The carbohydrates are very badly tolerated and many relapses are certainly due to their incautious use. The urine gives intense reaction to indican and to aromatic oxyacids. Examination of the Gram-stained fields from the stool of a typical example of this infection shows it to consist almost wholly of Gram-

* Read at the meeting of the American Pediatric Society, Washington, May, 1913.

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positive bacilli, presenting the morphological characteristics of the simple form of *Bacillus bifidus*. This organism can be readily cultivated; the *Bacillus infantilis* is obtainable from some, perhaps all, of the stools, and from the intestinal mucus it grows freely, sometimes almost alone when planted in fermentation tubes.

He further states that the very small number of Gram-negative bacteria to be seen in these fields is very striking. Herter's description of Gram-positive bacteria in the stools in such cases was corroborated by Panton in two of Hutchison's series. Apparently Herter would consider the cases explained by enteritis due to invasion by unusual bacterial forms.

French authors, Carnot, Arragas and Vinas, have dealt with the same phenomena, and have referred the food waste and resulting starvation to a primary impairment of the pancreatic function. And it is significant to note that cases analogous to the infantilism described by Herter as of intestinal origin have been reported by Bramwell and by Rentoul, and by them considered as due to failure of the pancreatic function.

From the study of a number of such cases, three of which are here reported, it has seemed to me that the apparently conflicting opinions as to etiology can be brought into unionism.

DUODENAL ORIGIN

There is evidence to support the contention that the primary lesion in these cases is an infective duodenitis with a secondary invasion of the pancreatic ducts and the production of pancreatic insufficiency, and the assumption of this theory has suggested a therapeutic procedure for the severe cases that seems worthy of further trial.

The rôle of the pancreas in fat-splitting is so well demonstrated that there is no need to quote the various physiologists and clinicians who have written on this subject. There seems to be a general consensus of opinion that if more than one-third of the fat ingested appears in the stools unsplit — that is, in the form of free fats — or even if such a proportion carries material quantities of fatty acids, the steapsin of the pancreas may be considered to be either insufficient or inefficient.

This view is opposed by Vaughan Harley who holds, from the study of a case of pancreatic obstruction, and from experiments on depancreatized dogs, that when excess of fat appears in the evacuations, diminished absorption, rather than deficient splitting, is the lesion. He came to this conclusion because, in his cases, a small proportion of fat was absorbed, but a large part of the waste appeared as fatty acids and soaps. He further feels that the pancreas has some internal secretion, as yet undiscovered, which is active in the absorption and utilization of fat, and this view is borne out by the experiments of Gross and of Falta. It is well understood that pathologic conditions in tissues other than the pancreas can lead to a large waste of fat in the stools. In acute duodenitis with

jaundice, in certain diseases of the liver in which biliary secretion is suppressed, in chronic tuberculous mesenteric adenitis, and in any acute enteritis, stools bulky with wasted fat may be encountered.

Talbot, in an interesting paper on tuberculous mesenteric adenitis, reports but one case in which the bowel movements contained any large amounts of free fat or fatty acids. In the major number of his cases, the fat excess was in the form of soaps, and his observations coincide with my own and with those of most observers. These findings indicate that the fat has been split, but that the absorption is inadequate. The few reported cases that show deficiency of fat-splitting can be explained on the ground that there is a partial or complete blocking of the pancreatic duct by that group of glands which lies about the head of the pancreas, where inflammation or enlargement might affect the duct by contiguity.

An interesting description of the rôle of the pancreas in splitting and absorbing fat, with an account of an unusual case of steatorrhea persisting from birth in an otherwise healthy child, one of whose five brothers was similarly affected, is contained in a paper by Garrod. The author assumes an inborn failure of fat-splitting power on the part of the individual reported on.

It seems also to be clearly demonstrated that one of the three pancreatic ferments, the lipase, the amylase, or the alkali protease may be diminished in quantity or power, while the other two secretions of the gland are doing their work in a fairly normal manner. A paper by Gross discusses this subject fully in its relation to the adult pancreas, but there seems to be no adequate study of the difference between the secretory power of the young pancreas and that of age.

The fact that bacterial invasion of the pancreas happens through the ducts as well as by the blood-stream, by the lymphatics and by contiguity (especially from infected mesenteric glands), is one of the best demonstrated facts in medicine, for acute suppurative pancreatitis, which one hears of rarely in childhood, has been reported to have been produced by the colon bacillus, the streptococcus, the staphylococcus, by mixtures of these two organisms, by the pneumococcus, by the bacillus of Friedlander and in rare cases by the typhoid and paratyphoid organisms. Invasion is determined by two facts: 1. By the production of much mucus at the ampulla of Vater, which causes partial blocking. It has been shown that under such conditions of stagnation the bacteria, especially motile bacteria, can readily ascend any of the body's various ducts. Bond's work on ascending mucus currents is of particular interest in this consideration. He has shown that when epithelium is damaged, inert particles can ascend ducts lined with mucous membrane, and he has suggested that this is a common mode of ascending infection by bacteria. 2. The second

determining factor was pointed out by Carnot, who has made a thorough study of pancreatitis. He demonstrates that blocking allows pancreatic enzymes to act on the epithelium lining the ducts and to soften and destroy it, and so provides pabulum for the organisms imported from the gut.

As long ago as 1898, Arraga and Vinas, in a detailed study, showed that it is not rare to encounter a more or less complete blocking of the pancreatic duct of children, with invasion of the duct by intestinal bacteria. Herter has shown, however, that at the level of the upper portion of the duodenum there are normally very few or no bacteria, and that these, when they do occur, are not of the pathogenic type. The inference is, then, that any invasion of the pancreas is secondary to a duodenitis in the presence of unusual bacterial forms in the upper gut.

BACTERIOLOGY

The type of case that this paper deals with cannot, of course, arise from acute suppurative pancreatitis, but if the possibility of ascending infections be accepted, as it is by all those who have carefully studied the matter, it is conceivable that bacteria of low pathogenic power ascending the ducts under like conditions will give rise to low grade of inflammation, followed by fibrosis, greater or less in degree. As a matter of fact, this is just what does happen, and such conditions found post-mortem in the pancreas have been attributed to invasions by colon bacilli of low resistance, to the staphylococcus, and to other pathogenic germs whose powers to damage their host had been minimized by residence.

On the other hand, organisms whose virulence is never great may establish themselves in the intestine. In the condition of acute and subacute infection already referred to as described by Herter, fecal fields instead of showing the normal preponderance of Gram-negative bacilli of the colon group, exhibit a bacterial flora similar to that seen in the stained fields made from feces of normal breast-fed nurslings. That is, the bacteria in these fields present the morphological characteristics of the simple form of the *Bacillus bifidus*. In some of these cases, a bacillus described by Herter and Kendall as *Bacillus infantilis* is present. There is some doubt as to the exact position this organism should take, and even Herter was of the opinion that it might possibly be a form of the *Bacillus bifidus*. Herter was interested in these cases chiefly because of the likeness the intestinal flora showed to the flora he found in those cases of infantilism that he studied and grouped as of intestinal origin.

The study of the stools in the group of analogous cases reported by Dr. R. G. Freeman, showed that in some the same types of *Bacillus bifidus* were predominant, and in others, one case in particular, Welch's *Bacillus aerogenes capsulatus*, occurred in preponderance with no *B.*

bifidus; in another, it was found in company with the latter organism and other bacilli.

When one considers that although steapsin is obtainable from the intestinal mucous membrane and from many other tissues of the body, the possibility of another lesion than that of the pancreas must be admitted in the case of those patients who waste fat so considerably, but that the pancreas should not be involved is unlikely even if other tissues are at fault. As a matter of fact, the post-mortem records of Arraga and Vinas reveal that in children who have shown such clinical pictures, there has been invasion of the ducts with evidence of chronic inflammation around the ducts; they describe the pancreas in these cases as being remarkable for the diminution of its volume, its increased hardness, its toughness on section and for definite marking out of its lobules in which the normal differentiation is markedly exaggerated. They say that throughout the essential tissue minute areas of degeneration and hemorrhage are found dotting the lining membrane of the ducts, and that there is a great increase of viscid mucus within these ducts. They describe the microscopic picture in these words:

> If we examine the duct of Wirsung at or near its entrance into the intestine, we are struck in many cases by the fact that the lining epithelium has almost disappeared. The wall of the duct is markedly thickened and is made up of fibrous striae surrounding collections of leukocytes. There is also in the new connective tissue a very marked increase in the number of blood-vessels, and these, for the most part, are unduly dilated. In the less severe cases, the process is not so advanced and we are able to see the epithelium in the process of degeneration; there is softening of the cells, with a fragmentation of the nuclei which gives rise to a poor staining reaction. Many of the cells are in the process of desquamation and are contributing to accumulations that block the ducts. A thorough examination shows that the degree of damage is proportional to the duration of the disease. From the finer ducts which have been attacked, widespread invasion of the parenchyma of the pancreas takes place, and is followed by a connective tissue increase. Following this increase of tissue, one finds secondary changes in the pancreatic acini, some of whose cells undergo softening, and others coagulation necrosis, with nuclei of lost contour, and poor staining quality. These lesions are most frequent in that portion of the pancreas neighboring the outlet of the duct of Wirsung. In those instances in which enteritis has been persistent and of long duration, a marked dilatation of the veins of the pancreas may be seen.

These authors look on the *B. coli communis* as the probable invader in these cases. They consider its motility as an important factor in aiding its entrance to the pancreas, but when we consider the work of Bond already referred to, there is no reason to doubt that any organism, motile or immobile, can invade the pancreas.

It seems perfectly reasonable, then, to assume that in the cases of patients whose stools show marked increase in free fat waste, definite depression of those digestive powers usually attributed to the pancreas, and in the stool a predominance of abnormal bacteria, the ducts of Vater,

and through them the pancreatic tissue, has been invaded by these abnormal organisms, and the pancreas has undergone an inflammatory reaction which has damaged the secretory power of the gland and impaired the digestive quality of its juice.

The autopsy of one of the cases here reported seems to warrant such an assumption, and the clinical findings in another also indicate the probability of this pathologic complex. The fact that many of these patients automatically recover is no argument against this contention, because it is quite conceivable that certain mild cases may be due to the establishment in the upper intestinal tract of a bacterium that maintains itself in this region with difficulty. Unless invasion of the pancreas occurred very rapidly, such an organism would find that the body had adapted its protective powers in the way that happens so frequently when the colon bacillus invades the urinary tract. Again, following dietetic measures, or the use of saline or mercurial purges, inflammation in the intestine may be allayed, mucus accumulations obstructing the outlet of the ducts cleared away, and the conditions which favor invasion of the pancreas by bacteria changed. The fact, therefore, that many cases have improved on simple dietetic treatment, or after the use of mercurial purges, is perfectly in accord with the view of the etiology here set forth.

The following examples of cases met in practice will be used to emphasize the contentions made in this paper.

CASE REPORTS

CASE 1.—Stella S., aged 22 months; weight 17 pounds. At the age of 1 year she suffered from an attack characterized by frequent, loose bowel movements, without pain, tenesmus or fever. This attack lasted for about ten days and she had no more trouble until February, 1911, when she had a recurrence of the same conditions in a more severe form; this attack had lasted for about three weeks when the child was first seen on February 27.

Physical Examination.—The child was then wasted and irritable. Hair was ill-developed and she had a distended belly; no fluid was found in the peritoneal cavity. The tonsils were not enlarged; there was no clinical evidence of lues; the Wassermann test was negative. The stools were characteristic, bulky, grayish-white, greasy bowel movements. The attending physician stated that she had had very marked starch waste.

She was put on a diet of 800 calories a day, provided through dextrins, skim milk, gelatin, scraped beef or white fish, maccaroni or rice, with green vegetables and fruits.

The report of the stool examination showed that on different occasions there was a great excess of free fat and fatty acids with some soaps; a moderate number of starch granules, both free and encapsuled were found. The blood showed 75 per cent. hemoglobin, 12,000 white cells, 58 per cent. lymphocytes, 42 per cent. polymorphonuclears; no parasites.

On July 20 there was no free starch in the stool; neutral fats and fatty acids were present in excess; the bacteria were predominantly Gram-positive; no colon bacilli.

August 29 a large amount of starch was being wasted; it seemed there was no fat in one examination, but the Gross casein method and Wohlgemuth starch test gave a very marked diminution in the amylase and protease of the stool.

September 6 there was a considerable excess of starch and of free fat; casein and starch digestion by the above methods was very much improved — from 100 units at the first examination, to 375 at the last. The child in the meantime increased in weight and well-being; her appetite improved and October 4 her weight was 24½ pounds. Since that time she has made a steady gain in weight and health and has shown no tendency to a recurrence. On the last examination of her evacuation by Dr. Alvarez, fourteen months after she was first seen, there was no excess of fat, free starch was not present, and the normal Gram-negative colon bacilli were reported as being predominant in the stool.

This is an example of a mild and temporary pancreatic insufficiency which is not at all uncommon to meet in infants of this child's age, and which, it seems probable, is due to a bacterial invasion of the intestinal tract and an ascending infection of the ducts of the pancreas. It is an upset which rights itself when under proper feeding conditions, the unusual bacteria give way to those normal to the small intestine, which under ordinary conditions are unable to grow with any amount of vigor so high up as the opening of Vater's duct. There are a number of cases in our history files which duplicate this in all its essential particulars.

The following case is an extreme example of the same condition:

CASE 2.—A. H. was first seen in his twenty-first month. Then he weighed 14 pounds, an increase of but 7½ pounds since birth. His mother's statement was that he had been breast-fed for the first four months, and that during this period he had gained one-half pound a week; from the fourth month he gained but little and at 9 months ceased to gain, but seemed contented and happy until during his tenth month he began to vomit; during the attacks he brought up at first food, and later large quantities of sour-smelling, bile-stained, watery material. There was then a period of improvement which lasted four months, although at that time he was on a diet that apparently contained about 5½ per cent. of fat. He then developed an alimentary intoxication, when he was seen by another physician who withheld all food save skimmed milk. Under this regime a slight improvement followed with a gain of a few ounces a week. At the age of 16 months he began to stand and was steadily gaining strength, up to his twenty-first month, when I first saw him in a vomiting attack similar to those already described.

Physical Examination.—The infant was found to be suffering from marked scurvy which rapidly disappeared when he was fed fruit juices. He was emaciated, with an exceedingly protuberant belly. Examination revealed nothing abnormal in nervous system, heart, lungs or abdomen, except marked distention, which was obviously due to intestinal gas. Neither spleen nor liver was enlarged; there was no fluid in the peritoneal cavity and no enlarged glands present. The blood showed no lymphocytosis, the hemoglobin was slightly diminished, no nucleated cells were present, but there were some alterations in the size and shape of the cells. The child vomited a large quantity of bile-stained fluid mixed with mucus and smelling of fatty acids. He would vomit from 1 to 2 quarts of this material daily during the attacks, which lasted from two to five days; during these periods the urine was scanty and concentrated. He had from two to three foul stools daily. When first seen these stools were scanty and composed largely of mucus; between the attacks of vomiting the stools were large and greasy, and contained large amounts of free fats and fatty acids. There was no starch reaction to iodin; no muscle fibers were found present; this examination was made some days after the child had been on a mixed diet of green vegetables, broth and scraped beef, with minimum amounts of

fat. The urine at this time and in subsequent examinations showed a heavy indican reaction, and Ehrlich's aldehyde reaction was positive, but neither albumin nor casts were found. On a mixed diet, with the exhibition of gray powder, ½ grain three times daily, the stools improved, the general condition was better and there was no further vomiting.

Management and Course.—In his twenty-eighth month the child suffered an attack of whooping-cough through which he passed uneventfully and from which he recovered without complications. After this he gained at the rate of about 1 pound a month until he weighed 18½ pounds. During this time no deficiency in the digestion of starch or protein was demonstrated by the Gross or Wolgemuth tests, but diminution in the pancreatic steapsin was to be inferred, as the fats were apparently entirely unsplit and unabsorbed. Unfortunately, no quantative determination of the relation between the ingested and excreted fat was made. Under the most careful and searching clinical observation by me and by Dr. Charles Minor Cooper, no indication of any complicating disease could be determined; the digestive tract only could be implicated.

The child's appetite was extremely capricious and it was difficult to get him to take a sufficient amount of food. On two separate occasions there was a definite color change in Fehling's solution when boiled with the urine. The change did not occur immediately and there was no true precipitation.

In his thirty-second month there was a very marked acceleration of all the symptoms. The patient, who had been improving and was allowed some freedom in diet, was seized with a characteristic diarrhea, having four to five stools a day. These were fetid, fatty-acid odored, greasy, and under the microscope they showed quantities of unsplit fat. This in spite of the fact that the fat was limited in the diet. During this attack, for the first time, starch appeared unaltered in the stools and meat fibers were discovered undigested, although meat was given in the form of very thoroughly scraped beef. At this stage an emulsion of raw sheep's pancreas was given with apparent effect. The child improved in strength and digestive power and returned to a limited degree of comfort, and again began to gain in weight. A light attack two months later was checked, whether spontaneously or through the aid of the pancreas emulsion, one is not certain. Pancreon (Rhananier), which it was attempted to give this baby, was always vomited. During the period of pancreas feeding, the pancreatic nuclei were always passed undigested and could be seen in great numbers in the stool.

At all examinations the fields of fecal flora showed a preponderance of Gram-positive cocci and bacilli which were reported as not unlike Boas Oppler bacilli, but smaller. At that time we attached no importance to the presence of these organisms in the digestive tract.

When the child was within a month of completing his third year he again became the subject of an attack which proved fatal. At this time he was not under direct observation, but the mother, a very intelligent observer, declared that on several occasions he passed voluminous stools of tarry material, which description seemed to indicate hemorrhage from the intestine, although the autopsy records showed that no blood was found in the intestine after death.

Necropsy.—The child died at 7:15 p. m., Sept. 18, 1911. Autopsy was permitted, but was not done until noon of the following day. The autopsy records state that the post-mortem revealed a very wasted child, the body in marked *rigor mortis*. On opening the belly, the intestines were pale and moderately collapsed. The ascending part of the duodenum was hard and seemed fibrotic. No fluid in the peritoneal, pericardial or pleural sacs; retroperitoneal glands slightly enlarged, not inflamed. Liver slightly decreased in volume, somewhat hard, spleen normal; right kidney larger than the left. The pancreas lay across the spine as a hard cord about the size of the little finger, was pale in color, but did not tear easily. Unfortunately, no examination was made of the papilla of Vater nor of the condition of the ducts. No enlargement of the mediastinal

or bronchial glands was found. Lungs free from adhesion, pale in color, did not tear easily, left apex firm to the touch, but floated in water. Heart in systolic contraction, normal.

Microscopic Examination (by Dr. William Ophüls).—Pancreas showed increase in connective tissue of septa; slight interlobular increase; pancreatic tissue was fairly abundant and seemed normal in appearance; there were many islands of Langerhans. Kidney showed slight increase of connective tissue in cortex; tubules normal; glomeruli normal. Lungs showed some areas of collapse where lining epithelium was cubical; otherwise normal. No abnormal changes in the intestine. Diagnosis: Pancreatic fibrosis; slight interstitial nephritis.

CASE 3.—This paralleled the last described in all the features except outcome. B. J. When the child was 13 months of age her mother noticed an abnormal distention of the abdomen; a week later vomiting with fever ensued and lasted two days; the stools, four to six daily, were then gray, smooth and voluminous. When first seen she was 17 months old. It was related that she was losing weight steadily.

Physical Examination.—The child was moderately grown, poorly nourished, much wasted; abdomen distended, not very full in the flank; bimanual examination made under anesthesia per rectum disclosed no tumors and no enlargements of the viscera. Reflexes, heart, lungs and throat normal. Blood, 10,200 white cells with a normal differential count. Hemoglobin 65 per cent. Von Pirquet tuberculin test was negative. Stools showed abundance of fats and fatty acids, some soaps, meat fibers, starch, dextrin and nuclei. Bacteria, Gram-positive bacilli in predominance. Urine usually normal; on two occasions showed slight sugar reaction; occasionally gave a marked indican reaction; the stools showed a moderate Ehrlich's aldehyde reaction; on a number of occasions a slight trace of albumin was present; at several times a few granular and hyaline casts were seen. Acetone was occasionally found during periods of starvation, and the same Gram-positive bacterium that dominated the stool was found in the urine several times; this was probably due to contamination. During the pancreas feeding an enormous amount of uric acid was reported as being present in the urine.

Course.—The child went progressively from bad to worse, and no food was tolerated by the intestine until Loefflund's malt soup, prepared with skimmed milk, was tried, and even with this aliment undigested casein was present in the stools. The weight fell steadily until it was less than 10 pounds. The clinical picture of extreme starvation with irritability was most pitiful. During this time the stools continued to show the Gram-positive bacillus in practically pure culture.

Bacteriology.—Dr. Alvarez' report is as follows: Escheric stain shows almost pure culture of a Gram-positive bacillus, often slightly curved, not as long as the Boas Oppler (probably not *Bacillus bifidus*). Fermentation tube culture shows a large amount of gas with a strong odor. Sediment shows a large number of the Gram-positive bacilli seen before and large amount of proteins; no signs of *Bacillus bifidus*. Acid bouillon shows no growth in ferment tube.

Emulsion of raw pancreas was given without apparent effect on the digestion; in fact, the amount of fat contained in the pancreas seemed to make matters very definitely worse, and unsplit fat appeared in the stools. With the hope of stimulating secretin, hydrochloric acid was now given without any change in the stools. Shredded pig's duodenum was now used in the attempt to provide a secretin, but without success.

Vaccine Treatment.—Dr. Walter C. Alvarez, to whom I am indebted for the laboratory examinations in this case, suggested that the constant domination of the stool by a Gram-positive bacillus was presumptive evidence of the pathogenicity of this organism, and proposed that an autogenous vaccine be prepared

and given to the child. This was done. The report of the first culture of this organism is as follows:

Culture on agar shows very minute white colonies which are apparently pure culture of the Gram-positive bacillus. They grow occasionally as long threads, or again as diplobacilli. On bouillon, the Gram-negative organism predominates by far. Transplant from agar to agar shows marked change to a thick diplobacillus sometimes so short as to be a thick diplococcus in chains; a few are Gram-negative and some may have spores.

The vaccine was prepared from the agar culture and every third day was given to the child in increasing doses, beginning with ten million. Up to this time the reports of stool examinations showed absence of diastase, low trypsin and practically no fat digestion; diastase was also absent from the urine.

No change was observed in the child for five days, when a fair amount of diastase was reported as being present in both stool and urine. The next examination, five days later, showed that there was still an excess of starch in the stool, but more than the usual number of Gram-negative bacilli, although there was still a large number of Gram-positive organisms. Subsequent examinations showed variations, diastase increasing in the stool, and starch varying from none to a slight excess, in one instance a large excess; free fat, fatty acids and soaps decreased in quantity, although whole milk was added to the dietary.

Three months after beginning the vaccine treatment, after about thirty injections, there were very few Gram-positive bacteria present, and the stool contained considerable soap. Five months after the beginning of the treatment, after an unremitting improvement, the child was able to take a normal mixed diet with a moderate amount of fat without any excessive waste; the stools showed simply a high predominance of soap, no wasted starch and a normal bacterial picture. By this time the child weighed 21½ pounds and was apparently in good general health.

CONCLUSION

It may be concluded then, that in the group of cases characterized by waste of most of the ingested fat, with or without loss of the ingested starches and proteins, we are probably dealing with a bacterial invasion of the pancreas secondary to the presence of an abnormal bacterial flora in the small intestine. The material here presented is too scanty to expect conclusions drawn from it to be accepted as final; the paper is prepared with the hope that others may consider it worth while to investigate the condition from this point of view.

The question of the value of vaccines in such a condition is brought up because in one case the results following the use of a vaccine were so striking that it seems impossible that mere coincidence will explain them. It is not suggested that one certain organism is specific for this condition. It seems quite reasonable that any pathogenic bacterium, or even the colon bacillus, under abnormal intestinal conditions, may become the inciter of a pancreatitis which may lead to a suppression or deficiency in one or the other of the pancreatic ferments.

Undoubtedly, a large number of cases in this group are mild and transitory and will respond to such dietetic measures as make the intestine an ungrateful field for the growth of the organism pathogenic in the particular case.

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STATUS THYMOLYMPHATICUS

WITH REPORT OF FOUR CASES IN ONE FAMILY *

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The condition that forms the subject of this paper can hardly be referred to as a distinct disease entity, yet it presents such a definite clinical picture, with more or less uniform pathologic findings, that it justifies classifying it as a disease state of special clinical significance.

Its nomenclature is influenced to a certain extent by the age in which the condition is observed, and by the predominance of certain clinical and pathologic features, yet as a whole the terms status thymicus, status lymphaticus, lymphatism and status thymolymphaticus are more or less synonymous. The reference further to the instances of mors thymica and thymic asthma are also closely related to this same condition.

Status thymolymphaticus is peculiar to children, but is also observed in the adult, and is characterized by a hyperplasia of the lymphatic tissues and of the thymus in association with a flabby, fat overgrowth of the body, hypoplasia of the heart and blood-vessels, particularly of the aorta, with a lowered constitutional resistance and a tendency to sudden death from trifling causes.

The four children in one family on whom this study is based, were observed by one of us (Goodrich), and presented the following clinical histories:

CASE HISTORIES

The father of these children is alive and well. The mother died of a heart and lung affection in October, 1910, some eighteen months previous to the death of the first child. In January, 1912, the father again married. In the father's family history there is a record of deaths of eight of his brothers and sisters, all under 9 years of age; three from scarlet fever, one erysipelas, one dysentery, and three from unknown causes. The mother's family history presents nothing of significance.

CASE 1.—April 8, 1912, Wyetta, the second youngest girl in the family, 4 years of age, died suddenly. For a few weeks some impairment of hearing had been noted, and her breathing had been somewhat difficult and stertorous, but this was ascribed to a cold and was treated with home remedies. About a year previously this child passed through an attack of diphtheria, during which she received 5,000 units of anti-diphtheritic serum. While she recovered very well from the diphtheria infection, she had not seemed as bright or active after this time. During a few days before her death this apathy was more marked. She manifested no desire to play and was greatly disturbed by enuresis, both diurnal and nocturnal. About midnight on the night before her death she aroused her father by an attack of choking followed by vomiting, after which she slept

* Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-Fourth Annual Session, held at Minneapolis, June, 1913.

until morning. On arising she was noticed to have a pallid look. She again vomited, was put back to bed, and the physician was summoned, but he found her dead on his arrival.

Necropsy.—Examination made by D. J. Glomset, twelve hours after death.

Record: Length of body 37 inches. The lips are pale. The abdomen is rather prominent. The cervical, axillary and inguinal glands are enlarged. The limbs are plump. The subcutaneous fat is well preserved. The muscles are pale. The peritoneal cavity is free from adhesions. The pleural cavities are free from fluid and there are no adhesions.

Thymus: The thymus is prominent and covers the right auricle completely. It fills the upper part of the anterior mediastinum and lies against the trachea, but there is no evidence of pressure on the windpipe. The organ is made up of two lobes. It measures 5 cm. in length, and 6 cm. in width. It weighs 42 gm.

Heart: The pericardial cavity contains a few cubic centimeters of a serous fluid. The right heart is dilated. The orifices are normal. There is a yellowish-gray nodule on the auricular surface of the anterior lip of the mitral valve. This nodule is about the size of a millet seed. The myocardium appears normal.

Lungs: The lungs are rather boggy, but crepitate throughout. The peribronchial lymph-nodes are enlarged, grayish-red in color and moderately firm. The largest is about the size of a large bean.

Alimentary Tract: Post-mortem changes are present in the stomach mucosa. Six inches above the ileocecal valve the upper part of the bowel has telescoped 2 inches into the lower. There is a hyperemia in the outer part of the bowel, but no signs of exudate or fibrinous adhesions. A large number of the mesenteric lymph-nodes are enlarged, varying in size from that of a pea to a hazelnut. Their consistency is rather firm and their cut surface is grayish in color.

Spleen: The spleen is enlarged, lobulated, and moderately firm in consistency. The malpighian corpuscles are prominent, but apparently lessened in number.

Case 2.—Eight days following the death of Wyetta, Louise, a bright and active 2-year-old girl, fell down the cellar steps fracturing her left clavicle. This was reduced soon afterwards by Dr. Goodrich. At this time she seemed bright and sat up in bed while the dressings were applied.

The general physical examination revealed a plump, well nourished child. The abdomen was somewhat prominent, liver and spleen not appreciably enlarged. No rachitic phenomena. The tonsils were large, and the cervical lymph-nodes were enlarged. The thymus was not palpable in the episternal notch, yet the percussion area corresponding to its location showed increased dulness. The following morning at about 7 o'clock she arose, and seemed quite well, eating, however, only a little cake for breakfast. Soon after 8 o'clock she was seized with a spasm, which was soon followed by another. Then she said she was hungry, and was given some strawberries, of which she ate quite heartily. She was then put to bed and was soon asleep. This did not last long, however, for she was shortly heard screaming. By the time her stepmother reached her she was dead.

Necropsy: Eight hours after death examination was made by Dr. D. J. Glomset.

Record: The body is very pale, a frothy liquid exudes from the mouth, and there are a few ecchymotic spots above the right eye. The cervical and inguinal glands are palpable. A trace of body heat is still present. The abdomen is prominent. Subcutaneous fat is well preserved. The abdominal muscles are pale. The muscles surrounding the left clavicle are infiltrated with blood. The clavicle is broken completely in two, one and one-half inches from the sternal end. The tonsils and adenoids are very much enlarged.

Thymus: The thymus is very prominent, covering the base of the heart and filling the upper and middle parts of the anterior mediastinum. It is composed of two lateral lobes and a central lobe, and measures 4.5 cm. in width, by 6.5 cm. in length. It is rather soft, grayish-white in appearance and weighs 54 gm.

Heart: The myocardium is soft and flabby. The right heart is dilated. There are two small yellowish nodules just above the aortic valve.

Lungs and Trachea: The mucosa of the trachea is congested, but there is no evidence of compression. A frothy fluid exudes from the cut surface of the lungs on pressure.

Liver: The liver is soft and has smooth surfaces. There are two yellowish spots present on the left border of the right lobe which extend about one-fourth inch into the substance of the organ.

Spleen: The spleen is about normal in size. It is distinctly lobulated and the malpighian corpuscles are strikingly prominent.

Stomach: Is moderately distended and contains a semifluid chyme. (This was sent to the chemist for examination, which proved to be negative.) Peyer's patches are prominent and grayish brown in color. The mesenteric glands are enlarged and range in size from that of a pea to a hazelnut. They have a moderately firm consistency.

Brain: Substance is very soft. The surface has a damp appearance. No gross pathologic changes.

CASE 3.—June 7, 1912, Walter, the only boy in the family, aged 5½ years, died in the same sudden manner as the two other children. Several weeks prior to this time, he, like his sister, Wyetta, was noticed to have some defect in hearing. On account of this, he was brought to the Children's Dispensary service of Dr. Goodrich on May 20, at which time the examination revealed a boy well nourished, sluggish mentally, having a pasty, adenoid appearance, "pot bellied"; the cervical, axillary and inguinal glands were all palpably enlarged. The tonsils were hypertrophied, adenoids were present. The spleen was moderately enlarged. The lungs were normal. The cardiac area was small. The thymus gland was not palpable in the episternal notch, but a distinctly broad area of dulness was demonstrable in the upper part of the sternum.

The urine findings were negative. Several attempts were made to obtain a blood examination, but were constantly opposed because of the fear of the simple prick with the needle that was necessary to secure the sample. A similar objection was made to an x-ray examination, or to the suggestion of its use as a therapeutic agent.

The patient was referred to the service of Dr. Pearson for a laryngoscopic and otoscopic examination, but the report was negative with regard to any abnormal findings. The clinical diagnosis of status lymphaticus was made at this time. A course of syrup of ferrous-iodid was prescribed, and the parents were admonished to watch the boy carefully for any change in his condition.

On the morning of the day of his death he seemed to be in his usual health, and had gone out into the garden amusing himself picking potato bugs off the potato bushes, when he was called inside because it was thought the sun was too hot for him. He went into the house and laid down on the bed, but said he was not sick. Soon after this on going to his room he was found to be dead. One arm had been raised over his head and a little bloody froth escaped from the mouth. His face after death, as in the other two children, had a mottled look.

Earlier in the day, this child had experienced some excitement; his sister had returned from school with her promotion card, this being the last day of school, and he became very much interested, so that he could talk of little else than of what he would do when he entered school in the fall.

Necropsy: Made twelve hours post-mortem by Dr. D. J. Glomset.

Record: Body plump, pale, and has a goodly amount of subcutaneous fat. The inguinal and axillary glands are palpable on both sides.

Thymus: The thymus is enlarged, moderately firm and weighs 25 gm. The tonsils are prominent, as are also the collections of lymphatics at the base of the tongue and in the pharynx. There is no evidence of compression of the trachea.

Lungs: There is marked edema of the lungs.

Lymph-Structures: The lymphatic structures of the small intestine are prominent. The mesenteric lymph-nodes are enlarged and moderately firm. The spleen is lobulated and the malpighian corpuscles are distinct. The heart is unchanged. The stomach and its contents were sent to Dr. F. J. Smith, professor of chemistry, Drake University Medical School, for examination as to the presence of any inorganic poison, with a negative result.

CASE 4.—July 7, 1912, just three months and four days following the death of the first, the last member of a family of four children, Florence, aged 7 years, succumbed to the same affection.

Since the death of the second child and more specially of the boy, Walter, she had been watched very carefully, not only by her family, but by her attending physician as well. She was examined frequently and presented the same physical changes that had been noted in the other children, as hyperplasia of the lingual and pharyngeal tonsillar tissue, the cervical, axillary and inguinal lymph-nodes. There was percussion evidence of an enlarged thymus, prominence of the abdomen, and a moderately enlarged spleen; the child was rather fat and flabby, had a pasty complexion, but seemed to be in good health. A blood and x-ray examination could not be made for the same reasons as in the other cases.

During the last two weeks of her life the "warning deafness" appeared. On two or three occasions in the week preceding her death, she was seized with spells in which she thought she was being choked, but recovered from them rapidly. In one of these seizures she said, "Oh, my God, someone is choking me." She then became cyanotic and sweat profusely; after recovering from it she asked her mother if she had seen all the people about her.

During the night previous to her death she became greatly alarmed because of the thunder storm then raging, but after its cessation she slept quite well. At 7 o'clock in the morning, as her father was going to his work, he awakened her, and as was his custom asked her how she felt; she replied "allright," and returned to sleep. Some two hours later she arose and went to the living room to dress, when it was noted that her head was dropped down on her chest; attempts were made to revive her but without avail and death evidently followed immediately.

Necropsy: Made twelve hours post-mortem by Dr. A. S. Begg.

Record: Body plump, pale, and has a liberal amount of subcutaneous fat. Abdomen is prominent; skin of thorax is mottled and cyanotic. The inguinal and axillary lymph-nodes are enlarged.

Thymus: Enlarged, moderately firm and weighs 40 gm. The dimensions are 4 by 5 centimeters. Marked hyperphasia of tonsils, lymphoid tissue at base of tongue, pharynx, and intestinal tract. Mesenteric nodes are enlarged. Spleen is moderately enlarged. There is some edema of the lungs. Heart is unchanged. No definite pathological change is found to account for death. The possibility of death being due to some chemical poison introduced into the stomach was excluded by a careful chemical analysis of the stomach and its contents after removal from the body.

Microscopic Examination.—The microscopical changes found in the lymph-nodes, spleen and thymus in all four of these cases are very similar and are those which occur in any chronic inflammation of the lymphatic system. There was a diffuse proliferation of the endothelial cells in all of the lymphatic structures. In Case 3 there was also an apparent increase of lymphocytes in some of the mesenteric lymph-nodes and in the thymus. In this case, however, the most marked change was an increase of the fixed cells of the lymph-nodes.

In Case 2, which is fairly typical of the others, the malpighian bodies of the spleen were partially replaced by endothelial cells. Only a few germ centers could be found in any lymph-node. There was a distinct increase in the supporting connecting tissue of the spleen and of the largest lymph-nodes. Giant cells were not to be detected.

In the second case there was also a rather marked degree of myocarditis, and in two of the children there was a diffuse atheromatous change in the aorta

of one, and on the mitral valve of the other. Hassall's corpuscles were prominent in all the thymi. There was a homogenous degeneration of the centers of some of the corpuscles of Hassall.

SUMMARY OF CLINICAL AND PATHOLOGIC FINDINGS

1. All the cases presented the same symptom-complex: pasty complexion, a flabby fat overgrowth, hypertrophied tonsils and adenoids, enlarged cervical, axillary and inguinal lymph-nodes and signs of an enlarged thymus; all were bottle-fed and had the "pot belly" of the rachitic.

2. Three of the four had a preliminary deafness.

3. Three of the four had seizures of choking or attacks suggesting thymic asthma.

4. All were apparently well nourished.

5. In all no malady sufficient to cause death was noted clinically.

6. In all cases death occurred before the arrival of a physician and under very similar circumstances.

7. No other similar cases are known among the playmates or friends.

8. All were of nervous temperament and became easily excited.

9. One child had diphtheria in 1911 and was given 5,000 units of antitoxin, the other three children receiving at the same time 1,000 units each for prophylactic purposes.

10. The post-mortem findings were practically identical in the four cases: the lymphoid hyperplasia and enlarged thymus prevailed in each. The weight of the thymi were, respectively, 42, 54, 25 and 40 gm.

11. The histologic changes found in all of the cases are extremely suggestive of a chronic inflammation affecting principally the lymphatic tissues. Whether this chronic inflammatory reaction has been produced by poisonous substances formed in some other part of the body or eliminated by some unknown micro-organism affecting the lymphatic tissues, is difficult to say.

12. It is difficult to conceive that the enlargement of the thymus was the main causative factor in the deaths of the children.

GENERAL CONSIDERATIONS

All discussions of status thymolymphaticus center about the conception of the pathological physiology of the thymus, and to a lesser degree of the lymphatic apparatus.

Sudden death has been frequently associated with thymic enlargement, the earliest mention of this fact being made by Plater in 1614.

All consideration of congenital and infantile stridor, asthma and sudden death has given to thymic enlargement, whether associated with coincident enlargement of the lymph-node or not, a clinical interest of considerable importance, about which an interesting controversy has been waged for a long time.

Paltauf[1] increased our knowledge of the subject when he described in 1889 a lymphatic constitution; he associated with status lymphaticus a hyperplasia of the heart and arterial system, and ascribed to it the condition of lowered resistance and increased tendency to fatalities in the various acute infections.

In a recent contribution on the pathology of the thymus by Wiesel[2] and the clinical discussion of status lymphaticus as exhaustively considered by H. Matti,[3] a most comprehensive view of the subject is obtained.

The anatomical status of the thymus cannot be said to be definitely fixed. Originally an epithelial structure, these elements gradually undergo various retrograde changes, but the epithelial remnants persist in the connective corpuscles of Hassall. At birth the lymphoid character of the organ is so marked that it is usually classed with the lymph-nodes. Some class it with the ductless glands; others place it without question among the lymphoid organs.

In many ways the thymus may be regarded as a homologue of the tonsils.

The estimation of thymus enlargement is subject to more or less error. Dudgeon[4] places the average weight of the thymus at from 7 to 10 gm. from birth to 2 years of age; Hart,[5] Friedleben[6] and Rolleston[7] also conclude that the acme of growth is reached by the end of the second year, then undergoes retrograde change, yet may remain stationary until puberty, which is followed by rapid physiological involution.

Glands weighing 20 to 30 gm. must be considered as enlarged.

The following tables of weights as collected by three different observers represent the variations peculiar to statistical studies:

Hammer[8]		Friedleben[6]		Von Sury[9]	
Age	Wt Gm.	Age	Wt. Gm.	Age	Wt. Gm.
New-born	13.26	1 yr. 9 mo.	20.7	New-born	14.4
1- 5	22.98	9-24	27.3	1 mo.	15.
6-10	26.10	2-14	27.	2-9	24.3
11-15	37.50	14-25	22.1	9 mo. 2 yr.	23.3
16-20	25.58	25-33	3.1	2-14 yr.	25.
21-25	24.73	.....	....	....	....
26-35	19.87	.....	....	....	....
36-45	16.27	.....	....	....	....
46-55	12.84	.....	....	....	....
56-65	16.	.....	....	....	....
66-75	6.	.....	....	....	....

1. Paltauf: Wien. klin. Wchnschr., 1889, ii, 877; 1890, iii, 172.
2. Wiesel: Pathologie der Thymus. Ergebn. v. Lubarsch-Ostertag 15 Jahrg., 1911, Suppl. 2, p. 416.
3. Matti: Ergebn. d. inn. Med. u. Kinderh., 1913, x.
4. Dudgeon: Jour. Path. and Bact., 1905, x, 173.
5. Hart: Grenzgeb. d. Med. u. Chir., 1909, 0, 321.
6. Friedleben: Physiologie d. Thymusdruse. Frankfurt, 1858.
7. Rolleston: Clin. Jour., 1898, xiii.
8. Hammer: Arch. f. Anat. u. Physiol. Anat., Suppl., 1906.
9. Von Sury: Vrtljschr. f. gerichtl. Med., 1908, xxxvi, 88, Series 3.

Hammer's weights are regarded as too high, and were mostly compiled from cases of accidental deaths. Lubarsch[10] claims that status thymicus is very rare in the new-born and young children.

Status thymico-lymphaticus is more frequently observed in older children and adults, thus strongly suggesting that it is an acquired postnatal condition.

The primary cause of thymic enlargement may be sought in any infection, intoxication or disturbance of metabolism, in which there is a

Fig. 1.—Photographs of the four children taken in October, 1911.

lymphoid or myeloid exhaustion. Sahli considers it a criterion of nutrition in infants, associating it with apparently well-nourished pasty children.

The enlargement of the thymus may be regarded, therefore, as a secondary process of the nature of a compensation.

10. Lubarsch: Jahreskurse f. Arztl. Forth., 1912, p. 56.

It may be associated with or without lymphatic enlargement. In the same light we are reminded of the observation of Kolisko[11] that the mesenteric glands and lymphoid tissues of the intestinal tract are often so prominently enlarged in enteritis of children as to completely obscure the primary inflammatory process.

In the anatomic findings of the four cases included in this paper, there is revealed principally a lymphoid and fibrous tissue hyperplasia that is very suggestive of a reactive process to some form of irritation.

The familial tendency peculiar to our cases has been noted by a number of other observers, Hennig,[12] Friedjung,[13] Perrin,[14] Hedinger,[15] Griffith[16] et al. Hedinger reports an instance in which five members of a family of nine children died suddenly, one of which came to autopsy with the usual findings of status lymphaticus.

Perrin reports in a family of eleven, nine children, and Griffith seven children in one family, from 1 to 8 months of age, who died suddenly with symptoms of dyspnea and cyanosis.

There is no record in the literature of any definite hereditary transmission of this condition.

Our knowledge of the physiology of the thymus is largely based on the experimental work that has been done, principally as the result of thymectomies in animals. The most extensive work is that of Klose and Vogt[17] and H. Matti,[18] from which the following facts are obtained.

Thymectomized dogs present several distinct stages:

1. A latent period of two to four weeks, during which there is no appreciable change.

2. A stadium adipositas continuing two to three months.

3. A stadium cachecticum of three to four months' duration.

4. Death usually within a year.

In addition, a marked change is noted in the general condition, the nutrition is retarded, growth is arrested and bony changes occur very similar to those of rachitis.

There is evidently a distinct connection between thymectomy and the process of ossification.

The removal of the thymus has a depressing influence on the sexual apparatus. A hyperplasia of the thyroid gradually occurs and also some hyperplastic change of the adrenals, hypophysis and pancreas.

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11. Kolisko: Handb. d. Aerztl. Sarchverst. Tätigkeit, 1906, ii, 701.
12. Hennig: Gerhard's Handb. d. Kinderkrankh., 1893.
13. Friedjung: Grenzgeb. d. Med. u. Chir., 1900, iii, 465.
14. Perrin: Ann. de méd. et chir. inf., 1903, vii, 217.
15. Hedinger: Deutsch. Arch. f. klin Med., 1905, lxxxvi.
16. Griffith: New York Med. Jour., 1909, xc, 444.
17. Klose and Vogt: Beitr. z. klin. Chir., 1910, lxxix.
18. Matti: Grenzgeb. d. Med. u. Chir., 1912, xxiv, 665.

Fig. 2.—The two older children (Cases 3 and 4). Photograph taken in April, 1912.

In the injection of thymus extract, Svehla[19] has demonstrated a pressor substance. Vincent[20] and Popper[21] report similar results, while Oliver and Schafer[22] and Morehead obtained negative results.

Thymus feeding has not led to any definite results, and the third attempt to produce a state of hyperthymization by means of thymus transplantation, carried out mainly by Sommer and Florken[23] and Ranzi and Tandler,[24] has also not given any reliable or uniform results.

From the experimental results reported, it is evident that dethymization is attended by rather definite systemic disturbances, particularly in the process of ossification and growth of bone, but the opposite state of hyperthymization is by no means as clearly defined.

The apparent association with the chromaffin system is evident, and in the opposing as well as controlling influence of thymus extract on the secretion of the other ductless glands, there is strong suggestion of a separate internal secretion of the thymus, yet it still lacks much corroborative evidence.

In connection with the hyperplastic changes in the thymus and the lymphatic apparatus, some interesting findings have been observed in other organs.

Wiesel refers to the presence of thyroid enlargement in status thymicus. The association of Basedow's disease with status thymolymphaticus has been demonstrated in a large number of instances by Capelle.[25]

The larynx is often small and of the heterosexual type.

The hypoplasia of the aorta, as well as its branches, and the small heart have been referred to. Von Neusser[26] has called attention to abnormal length of the bowel and atypical lobulation of the lungs. Shiota[27] has reported the occurrence of an abnormally long appendix vermiformis. Wiesel[28] has found hypoplastic adrenals in well-marked examples of this condition, and the interesting contribution of Hedinger[29] corroborates the coincidence of Addison's disease with status thymolymphaticus.

In a careful study of fifteen cases of Addison's disease he found eight instances of status lymphaticus, four cases of status thymolymphaticus

19. Svehla: Arch. f. exper. Path. u. Pharm., 1900, xliii, 321.
20. Vincent: Arch. Physiol., 1904, xxx, 16.
21. Popper: Sitzungsber. f. Acad d. Wissensch. Wien., 1905, cxiv, 539.
22. Oliver and Schafer: Cited by Matti, Ergebn d. inn. Med. u. Kinderh., 1913, x; Morehead: The Practitioner, 1905, lxxv, 733.
23. Sommer and Florken: Sitzungsber. d. physiol. med. Gesellsch. Wurzburg, 1908, 3 and 4, p. 45.
24. Ranzi and Tandler: Wien. klin. Wchnschr., 1909, xxii, 980.
25. Capelle: München. med. Wchnschr., 1908, p. 1826.
26. Von Neusser: Zur Diagnose der. Status thymico-lymphaticus, Wien, 1911.
27. Shiota cited by Matti: Ergebn d. inn. Med. u. Kinderh., 1913, x.
28. Wiesel: Virchows Arch. f. path. Anat., 1904, clxxvi, 103.
29. Hedinger: Frankfurter Ztschr. f. Path., 1907, i.

and three cases incomplete. These observations have been corroborated by Warthin,[30] Pappenheimer[31] and others. Bartel[32] has associated glioma of the brain with the condition under discussion. Marie[33] found acromegaly with status thymicus. Von Recklinghausen reported the presence of status thymolymphaticus in a case of osteomalacia.

The association of a lymphatic constitution with rachitis has been frequently emphasized.

The sudden death in status thymolymphaticus, which forms such a tragic chapter in this condition, has been variously explained, and continues to be a problem of considerable controversy and discussion.

The several theories that have been proposed may be grouped as follows:

1. Mechanical: pressure of enlarged thymus on the trachea or contiguous blood-vessels, causing stridor, asthma and death.

2. Intoxication due to faulty tissue changes similar to the action of syphilis on the heart muscle (Paltauf).

3. Hyperthymization resulting from pathological increase of an internal secretion, both of the thymus and of the lymph-nodes.

Paltauf's explanation has been largely discarded in view of the lack of any supporting evidence.

The mechanical theory is also not sufficient, as so many of the cases show no previous signs of thymic asthma.

Until the existence of an internal secretion has been more definitely demonstrated, it will not be consistent to attribute thymic death to a state of hyperthymization. On the other hand, a critical review of the literature, giving due consideration to all anatomic relations, a mechanical thymus death by tracheal compression, in rare instances also by compression of the blood-vessels, is a distinct possibility, and in a number of instances has been definitely proved to be the cause of death.

Birchner[34] has demonstrated by experimental means the toxic effects of injections with pathologic thymi.

In adults a cardiac death is the rule, and it seems proper to refer to a "thymic heart" in the same sense that the term thyroid heart is used.

Again, it is not so much the thymic hyperplasia as the coincident unfavorable factors that attend this state, which are probably largely to blame for the fatal outcome. The death is often induced by a number of influences that have no effect on the normal individual.

30. Warthin: Arch. Pediat., 26, 1909, xxvi, 597.
31. Pappenheimer: Jour. Med. Research., 1910, xxii.
32. Bartel: Wien. klin. Wchnschr., 1908, 783.
33. Marie: Gaz. d. hôp., 1893, lxvi, 202.
34. Birchner: Centralbl. f. Chir., 1912, No. 5, p. 138.

DIAGNOSIS

The recognition of status thymolymphaticus should present no difficulty, since the associated symptom-complex is usually so well defined. Unfortunately, in the past the attention was not directed toward these unfortunate patients until after a sudden death had occurred.

It should be possible to detect complete as well as incomplete types before the fatal exitus manifests itself.

TREATMENT

This resolves itself into prophylactic and curative. Under the former should be emphasized:

1. Avoidance of excitement.

2. No surgical operation unless absolutely necessary, as these patients do not take any kind of anesthetic well.

3. Very warm or very cold baths are to be avoided, as the shock has been known to cause death. Cases of sudden death while swimming may be ascribed to this cause.

4. Prevention of infection, especially of the upper respiratory tract.

5. Securing good hygienic conditions of life.

As regards the curative treatment of status thymolymphaticus, it can hardly be considered as curative in its true sense, since it is more of an attempt to treat and relieve certain symptomatic manifestations of the condition. A medicinal or internal form of treatment is not applicable at all. Of the non-medical therapeutic measures, mention should be made of the following:

1. Intubation with a long tube reaching to the bifurcation of the trachea, being of special value in cases of thymic pressure.

2. Thymectomy, partial or complete, is an operation of considerable surgical risk, yet carried out successfully by Rehn,[35] Veau and Olivier,[36] and more recently by Jackson[37] in this country.

This operation has for its purpose the relief of thymic pressure and removal from the system of the toxic influence of a pathological thymus.

3. Radiation. The use of the Roentgen ray has been espoused by Friedlander,[38] Heinecke[39] and Regaud and Cremieu,[40] and all report brilliant results in producing involution changes in the enlarged thymus. This agent will be equally effective in reducing the size of the spleen and the hyperplastic lymph-nodes.

Because of greater safety and evident efficacy its use is to be recommended.

35. Rehn: Arch. f. klin. Chir., 1906, lxxx, 468.
36. Veau and Olivier: Jour. de méd., March 15, 1912.
37. Jackson: Jour. Am. Med. Assn., 1907, xlviii, 1753.
38. Friedlander: Arch. Pediat., 1911, xxviii, 810, No. 10.
39. Heinecke: Grenzgeb. d. Med. u. Chir., 1905, xiv, 21.
40. Regaud et Cremieu: Thèse de Lyon, 1911.

NEEDLE IN THE HEART FIFTEEN MONTHS; DEATH; AUTOPSY *

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CASE: *R. Z., aged 2 1/4 years, under observation at the Presbyterian Hospital, N. Y.; accident when 1 year old; died; autopsy.*

A puny, undersized child was brought to the out-patient department of the University and Bellevue Hospital Medical College, the parents hoping that she might be strengthened, her color improved, her bronchitis cured. She was announced to me among the material for clinic as "congenital heart disease." She was not cyanotic. I put my hand over her chest and felt the purring thrill. I presumed it to be a case of congenital heart in which there was no cyanosis, an exception to the rule. On further examination it was noticed that the murmur, though loud and purring, was heard all over the chest, and was not of maximum intensity over the left space and costo-sternal junction. The maximum was rather over the belly of the left ventricle. The physical signs were exceptional and not at all convincing; but since the child was so young and had no previous history of illness, it was presumed that it must be really a case of congenital malformation without cyanosis. The unclassical points here mentioned led me to make an effort to get the child into hospital for further observation. When it arrived at the Presbyterian Hospital I went through the same preamble to the staff. After two examinations I asked for a radiograph, to learn the size of the right ventricle and for any chance information that might be gained. The accompanying illustrations show what the x-ray revealed (Fig. 1). One plate exposure caught the heart just in contraction and gave two parallel shadows. Two right-angle exposures located the foreign body in the cavity of the left ventricle.

Amusing stories are told of the weird effect that the first developed plate had on the photographer. It is said that he believed the plate had a defect in it; that in the second plate the camera was defective; in the fourth and fifth and subsequent plates that his brain was touched. I cannot vouch for these stories.

Now that the diagnosis was made, the question arose, How was the needle to be removed? While the surgeons were discussing the matter the child developed bronchitis. She recovered from this, and after

* Read before the American Pediatric Society, Washington, D. C., May 7, 1913.

remaining in the hospital for a month or more, it was thought best to remove her to the country. There was no hope for the removal of the needle and really no hope of the child's living in her present condition. After a short sojourn in the country the child returned suddenly to the hospital with pneumonia, and died within twenty-four hours and consequently was a coroner's case.

The coroner made a most careful and thorough autopsy, and I am able to give a completed history. The needle was found as predicted, free in the left ventricle, butt-end down (Fig. 2). The needle was slightly corroded. There was no ante mortem clot and no inflammatory action about it. It pierced and extended beyond the mitral valve and scratched the endocardium of the auricle. In the auricle there was an area of superficial ulceration where the point of the needle had rubbed off the endothelium. The apex of the heart was adherent to the pericardium about the region through which the needle went, for an area the size of a quarter of a dollar. There was also a little roughening of the pericardium about the adherent area. This was the sum total of the irritation which the needle gave in its travel through the diaphragm and pericardium. On the under-side of the diaphragm was a streak of rust or dark staining (Fig. 3), showing the course by which the needle had traveled from the abdominal cavity to the ventricle.

The needle entered the abdominal cavity by way of the skin surface, presumably at the time of the fall at the age of 1 year. By one thrust it was shoved into the very apex of the heart, the butt-end of the needle remaining just within the skin of the abdominal wall, the point possibly extending even into the cavity of the ventricle. The point of entrance into the skin was at the most exactly near point, viz., at the left side of the ensiform cartilage close up to the ribs; likewise, the exact point of entrance into the apex was at the septum. The direction of the needle was such as to miss the right ventricle and proceed straight to its resting place in the left heart. There was no evidence that the needle had touched the liver or done injury to any other abdominal tissues or organs. After the first thrust, it is easy to know its mode of advance. Every muscular contraction sent it forward on its way, point foremost, till it lay free in the cavity of the heart. The butt-end was free in the cavity's apex, and since the needle was longer than the cavity, the point extended up into the auricle, as mentioned above, thrust through the one leaf of the mitral valve.

There is but little authentic history, but this is a summary of what the parents gave. The child was, on entrance, 2 years old. When 1 year old, it fell out of a wooden cradle. At that time the mother noticed a protrusion just below the ensiform cartilage in the mid-line, "like a nail," "as if the child had swallowed something," but the mother knew

nothing of anything swallowed. She said that she took her to a doctor who felt the swelling, but said it would go down, and so it did. There was no abrasion of the skin anywhere. The fall gave no severe results at the time, though the mother says that since that time the child has gradually failed. In one conversation there are stray remarks that the swelling did not come till two weeks after the fall; that there was pain; that she took her child to the doctor for pain, and that there was stomach

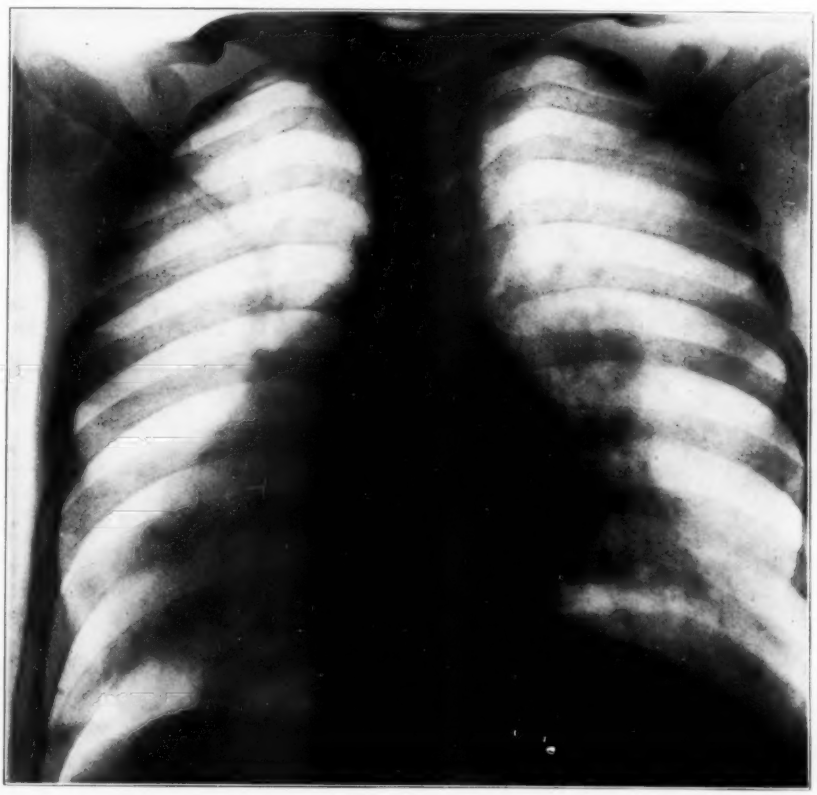

Fig. 1.—Needle fifteen months in the left ventricle of a child 2¼ years old.

trouble. One cannot doubt that there may have been pain and gastric disturbance, but in that class of observers exact details are not forthcoming. It may be believed that there was protrusion ("swelling") in the epigastrium; that there was "fever," considerable "heaviness of the chest"—dyspnea, especially at night.

The hospital historian recapitulates as follows: Chief complaints, heaviness of the chest, at night; paleness; diagnosis, congenital heart lesion.

Twelve days after the child was sent to the country to build up its strength and blood, it returned with symptoms of pneumonia, and the same day it died. An autopsy was made. The photographs show the needle in position.

While this case was the absorbing topic of conversation, a patient waiting in the hall heard something said which stimulated the father to offer a remark of interest in this connection. "Why, my baby had a

Fig. 2.—Needle in the left ventricle; point stuck through the mitral valve; butt-end is within the cavity of the ventricle.

needle in her belly," he volunteered. "The nursemaid had a needle and thread stuck in the shoulder of her dress. She was dandling the baby up and down on her shoulder," peering, no doubt, far out the window to see the nearest policeman on the beat. "All at once the needle was gone, the child failed to be quieted by the dandling on the shoulder, and when it came time to put the child to bed there was noticed to be hanging out of the belly a thread. On pulling at the thread, out came a little more

thread and finally a needle. This conversation was volunteered, was repeated verbatim by each of the parents separately, and not in each other's presence. We purposely made little of the incident, and when they were not in the sight and hearing of each other, we asked them about it as though it were not of the least importance, and the father and mother repeated the same story in the same words. Both had been present at the extraction of the needle and thread, and both told the same story.

However the needle in the case here reported started on its way, there is no mystery as to its method of progression. Like all needles in

Fig. 3.—Needle in the left ventricle. Dark line near the measure is the scar showing the track through the diaphragm.

the tissues, it progressed point first, each step being in time with some muscular contraction.

How the needle came to be in position to pass by one clean thrust from the outside world quite out of sight within the integument, is of course entirely conjectural. A nurse has suggested that some people prefer to sew the garments on rather than use safety pins. In such a case it is quite within the range of possibility that a needle was left in the diaper ready to be thrust forward as the child fell over the crib.

It is of little value to discuss the physical signs of this unusual lesion. However, the murmurs were of nearly every variety. Over the belly of the ventricle the murmur was double; at the apex it was loud systolic; at the base it was also systolic and loud. The heart was large.

The condition of the needle was also of interest. One might suppose that the needle would be much corroded and that an ante mortem clot would be found. On the contrary, there was but little corrosion. As seen in the picture, there were little beads along the shaft, but not much. There was no sign of clotting before death.

The needle was the ordinary one used in sewing coarse garments, or, more properly, undergarments. It was about two inches long. It traveled by the shortest route possible from the outer world to the ventricle. It seemingly entered at the side of the ensiform cartilage, went straight to the apex and so on to its place in the ventricle.

It is useless to discuss the possibility of its removal during life, and yet it was a fascinating ground for speculation at the time. A powerful electro-magnet was suggested by more than one. There was no hope for the child without surgical interference, and the needle had been in place for more than a year. It was also quite true, as the mother said, that the child was remaining stationary or losing ground in spite of the best of care. In short, there was little or nothing to lose by operation, and possibly something to gain. However, there was no operation, and in the light of the autopsy findings, it is fortunate that there was none. The parents, I might say, were quite willing to have anything done that the surgeons could recommend. In fact, they threatened to take the child out and possibly try elsewhere if something was not done, which, being interpreted, meant an operation.

The child was in the hospital three months, became quite content with her surroundings, and yet she had these peculiarities to the very end. She never spoke a word to any one of the staff for two months, did not smile in that time, yet was quiet, sat up in bed and after the first few examinations and visitations, never cried. She was a weird little thing, sitting in her crib looking straight forward into the eyes of all callers, as though she but faintly saw them.

57 East Seventy-Ninth Street.

THE DIAGNOSIS OF INTUSSUSCEPTION BY X-RAY

IRVING M. SNOW, M.D., AND MARSHALL CLINTON, M.D.
BUFFALO, N. Y.

The following case presents so many points of interest that it is herewith reported:

History.—The patient was the third child of healthy parents, born after a normal labor. She was nursed, but the mother suffered from sore nipples so much that she cried each time the child was put to the breast. When the child was 5 weeks old it vomited a clear bloody fluid and some hours afterward passed a black, tarry stool, but showed no other evidence of illness. It was supposed that the infant had swallowed blood from a fissured nipple, but the mother immediately withdrew some clean milk with a breast pump, and it is possible that the symptoms were due to a slight intussusception which was spontaneously released.

For the next few weeks the baby was fed from the breast, but the milk began to diminish and it was given supplementary feedings of cow's milk and a malted food.

November 6. The child was now 3 months old; it took the bottle well at 3 a. m., and afterward slept. At 6 a. m., it refused the breast and seemed quite ill. The child commenced to cry with pain, vomit and pass frequent stools of mucus and blood. The fifth vomiting attack showed regurgitation from the small intestine.

Examination.—At 8 a. m., a rectal examination was made with negative results. Directly after the withdrawal of the finger a quantity of fresh blood flowed from the anus. The abdomen was relaxed and on palpation a sausage-shaped tumor, moveable and insensitive, was felt in the left upper abdominal quadrant. The temperature was normal, the heart strong and regular. No medicine was given and feeding was stopped.

Diagnosis.—Dr. Edgar McGuire saw the infant in consultation at 10 a. m., and considering the positive symptoms present, colic, vomiting, bloody stools and a tumor in the upper abdomen, agreed with the writer (Snow) that the child was suffering from intussusception. As Dr. Marshall Clinton had been selected to operate, to relieve the child, a warm, normal salt solution was injected under pressure into the rectum.

Following this the child became easy and comfortable and slept. The vomiting stopped and the bloody mucous stools ceased, and when Dr. Clinton examined the patient at noon it was impossible to outline the abdominal tumor. This disappearance of the tumor is explained by the

Fig. 1.—Bismuth filling large intestine up to beginning of the intussusception; small amount of bismuth in dilated small intestine above constriction.

Fig. 2.—Bismuth forced under pressure alongside intussusception, filling large intestine up to ileocecal valve.

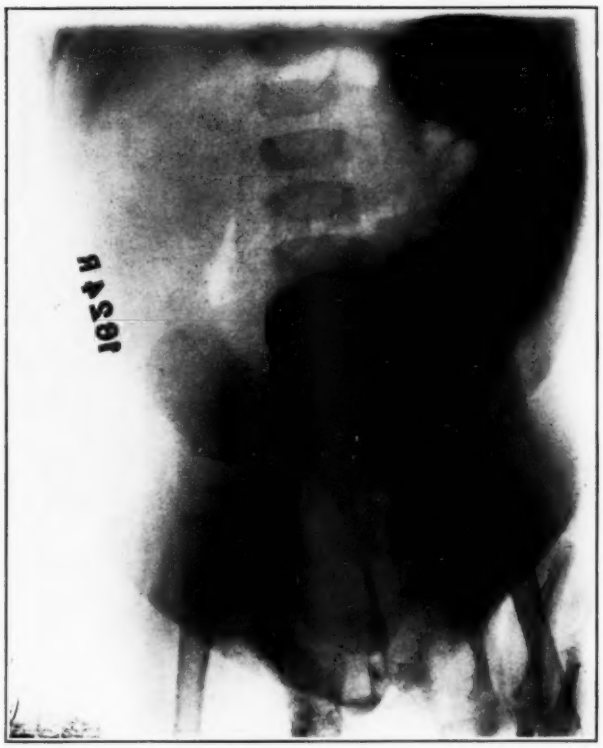

Fig. 3.—Dr. Parmenter's case of intussusception. Plate taken as soon after injection as possible, showing the obstruction at the splenic flexure.

Fig. 4.—Plate taken about three minutes after plate in Fig. 3, showing some of the bismuth forcing its way beyond the splenic flexure.

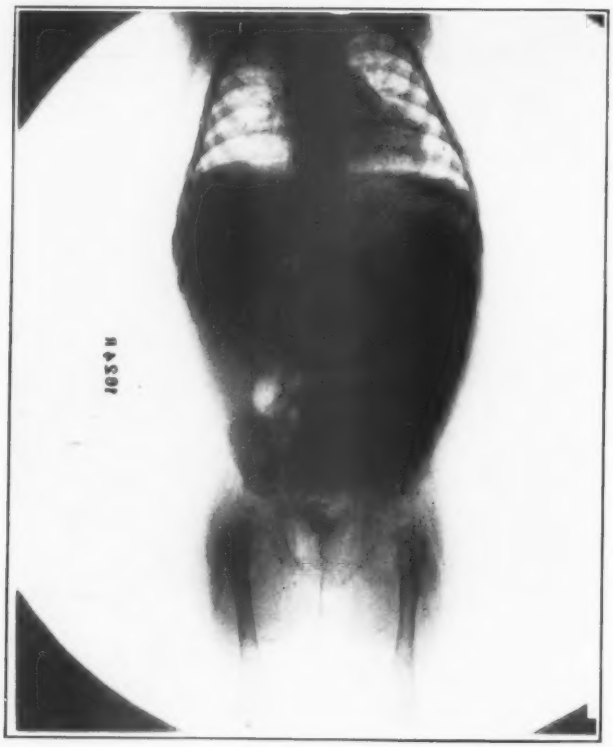

Fig. 5.—Plate made five minutes after plate in Fig. 4, and ten minutes after the injection, showing bismuth passing into the large intestine around the intussusception.

Fig. 6.—Plate made ten minutes after plate in Fig. 5 showing still more bismuth passing through.

progressive shortening of the mesentery which pulled the mass of gut to the post-part of the abdomen.

It was, nevertheless, decided that the intussusception was not reduced and suggestion was made that a radiograph be made with the colon filled with bismuth emulsion.

At 4 o'clock the child was taken to the office of Dr. Leonard Reu, where two pictures were taken, after injecting the colon with bismuth and acacia mixture; an additional amount of bismuth was injected between the first and second exposures.

The patient did not suffer from this manipulation and was taken home apparently undisturbed.

The radiograph showed an unreduced intussusception in the right upper quadrant of the abdomen. A small amount of bismuth emulsion had been forced through the gut above the point of constriction.

Late in the afternoon the temperature was 101 F., pulse 150, and the baby passed a bloody mucous stool.

At 7 p. m. the child was taken to the Buffalo General Hospital, where an operation was performed by Dr. Clinton.

Operation.—After iodin preparation of the abdomen and the administering of a minute hypodermic of morphin, under ether anesthesia, the abdomen was opened in the median line just above the umbilicus for 1½ inch. The abdominal wall was infiltrated with a 1 per cent. solution of novocain and then a 1 per cent. solution of quinin and urea hydrochlorid.

The intussusception was located by touch, and with two fingers the intussusception was squeezed out, with no attempt to bring it outside the wound. The invagination was ileocecal, ¾ inch of ileum being jammed into the cecum and colon.

After reduction, which was easily performed, the ileocecal junction was brought into the wound and three mattress sutures were placed in the sides of the ileum and the wall to try to prevent a recurrence. A further infiltration of the peritoneum with urea solution was made before closing the wound, which was sewed up in layers in the usual way. Time of operation, twenty minutes. Time of operation after the onset of symptoms, thirteen hours.

After-Course.—After the operation the child was taken home and 2 drops of paregoric and 2 teaspoonfuls of water were given per rectum every hour during the night.

Next morning the baby passed flatus freely and considerable bismuth mixture. Temperature, 100.4; heart rapid but strong. Child comfortable and had lost but one-half pound in weight.

There was a rapid convalescence, but as the mother's milk failed, and as cow's milk disagreed, it received and throve on condensed milk. At 7 months of age, 4 months later, the weight was 20 pounds.

The case was observed practically from the time the invagination occurred until operative relief thirteen hours later.

After giving a saline injection a deceptive amelioration occurred. All symptoms disappeared and the condition was masked for several hours until a radiograph was made.

An additional case of intussusception diagnosed by x-ray is reported by Dr. J. Fred Parmenter as follows:

History.—G. B., aged 9 months, entered the Children's Hospital May 7, 1913, suffering from facial lupus vulgaris and malnutrition. Family and past history negative.

Present Illness.—June 17, 1913, after passing a good night and seeming in perfect health, the infant took food at 8 a. m. and had a large, yellow, normal stool at 9 a. m. At 10 a. m. the child suddenly vomited a large quantity of food and began to look quite ill. At noon, during rounds, a nurse called attention to the child, from whom she had just removed a bloody diaper. Abdominal examination showed a rather tender mass on the left side just below the umbilicus. Diagnosis of intussusception, and immediate operation advised, which was accepted by the parents.

Radiographic Diagnosis.—At Dr. Snow's suggestion radiographs of the colon were made at 1:30 p. m. by Dr. Leonard Reu, the bismuth solution being introduced per rectum, which verified the clinical diagnosis, as the accompanying plates will show, Dr. Reu's interpretation being as follows: Plate (Fig. 3) taken as soon after the injection as possible, one to two minutes, shows the obstruction at the splenic flexure. Plate (Fig. 4) taken about three minutes later shows some of the bismuth forcing its way beyond the splenic flexure. Plate (Fig. 5), five minutes after No. 2, and about ten minutes after the injection, shows more bismuth passing into the large bowel around the intussusception, while Plate (Fig. 6), taken ten minutes later, shows still more bismuth passing through. Patient's condition immediately improved after the injection, this being due to the slight temporary relief of the obstruction, which was producing shock. The patient vomited and had several bloody stools before the operation, which was performed by Dr. Parmenter, assisted by Dr. Joseph Lewis, at 3:30 p. m.

Operation.—Ether anesthesia. Iodin preparation, high median incision; intussusception found on left side, just below the splenic flexure, was delivered and reduced by gentle taxis and pressure on the colon side as suggested by Moynihan. The cecum and ascending colon were practically devoid of mesentery, which accounted for finding the tumor so early on the left side. It was deemed advisable to remove the appendix, which was done, and the abdomen was closed in the usual manner. The intussusception began at the ileocecal valve, and several inches of ileum were telescoped into the colon as far as the splenic flexure. Duration of operation eighteen minutes; uneventful recovery, to date, ten days.

The case is reported because of the opportunity afforded of making an early diagnosis and the unusual location. The intussusception was immediately diagnosed and operated on six hours after commencement of symptoms.

Inasmuch as the life of a patient with intussusception depends on an early diagnosis, and as the clinical picture may be atypical, with some important symptoms lacking, as abdominal tumor or intestinal hemorrhage, the aid of the x-ray in the diagnosis of suspected intussusception should come into common use.

As far as we are aware, ours is the first reported case in which a radiograph was taken to confirm the diagnosis of an intussusception.

476 Franklin Street.

MUCOUS CYST OF THE CECUM IN AN INFANT TEN WEEKS OLD, PRODUCING OBSTRUCTION OF THE ILEO-CECAL VALVE AND SYMPTOMS SIMULATING AN INTUSSUSCEPTION *

A. D. BLACKADER, M.D.
MONTREAL

For the privilege of reporting this very interesting case I am indebted to the courtesy of my confrères in the Montreal General Hospital, Drs. J. M. Elder and A. H. Gordon.

History.—Chas. H., aged 10 weeks, was first seen in consultation by Dr. Gordon March 9, 1913, for continued vomiting. The infant had been nursed by its mother and had thriven well for the first two months of life. Then it began to vomit after taking nourishment. The physician who first saw it regarded the mother's milk as the cause of the trouble and advised artificial feeding. This was tried without benefit; the vomiting persisted and the nutrition failed rapidly. There was no pyrexia. When Dr. Gordon saw it in consultation he recognized a sausage-shaped tumor in the left lower right quadrant of the abdomen and recommended immediate operation. It was at once brought to the Montreal General Hospital and placed under the surgical service of Dr. Elder.

Examination.—The notes on entrance are as follows "Infant, 10 weeks old, well developed for age; nutrition poor; very little subcutaneous tissue; no glandular enlargements; lungs and heart normal; abdomen distended. In the right lower quadrant is a sausage-shaped tumor, distinctly palpable, 3 inches long by about 1 inch in diameter, freely movable, not tender; no muscular rigidity of abdominal walls. Distinct peristaltic waves are noticed traveling toward the site of tumor. Temperature 99, pulse 140, respirations 40."

Treatment and Course.—Shortly after entrance into the ward a high enema was given which brought away no flatus, and only a small amount of feces, in which there was no appearance of blood or much mucus. Following this the abdomen was immediately opened by Dr. Elder under spinal anesthesia. The oblong tumor mass was found to involve the lower portion of the ileum and cecum; above the mass the ileum was much distended, while below it the ascending colon was collapsed. Regarding it at first as an ileocecal intussusception, careful efforts were made at reduction, and when they failed, a resection was performed with end to end anastomosis, and the abdomen closed. On examination afterward of the incised mass its true nature was disclosed.

The child had no symptoms of shock after operation and for several days its condition was good. On the third day the temperature fell to normal, the abdomen was soft, the bowels moved freely and the infant was placed under my charge for its feeding. On the tenth day after the operation, however, the pulse became weaker, the face assumed an earthy hue, the features became drawn, and on the morning of March 24, twelve days after the operation, death occurred from peritonitis.

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* Read at the meeting of the American Pediatric Society, Washington. D. C., May, 1913.

*Submitted for publication June 22, 1913.

Pathologist's Report.—The pathological report on the specimens removed at operation was as follows: "The tumor consists of the lower portion of the cecum with its contained cyst, and the appendix. The cyst, much collapsed, measures about 2 cm. in diameter, is unilocular, contains glairy mucoid material and is situated on the wall of the cecum opposite the ileocecal valve, extending over to and completely obstructing that orifice."

Microscopical Examination.—Microscopic examination of the cyst walls showed the surface of the tumor projecting into the lumen of the cecum to be covered with mucous membrane similar to that of the intestine; the cyst to be lined with a somewhat stretched layer of columnar epithelium which, however, in some places was folded into gland formations. Beneath each surface of epithelium was a submucosa infiltrated with lymphocytes, and between these again are three more or less distinct layers of muscle.

Diagnosis.—From this report the cyst was regarded as in all probability a retention cyst, arising either from some fault in development or from an inflammatory occlusion of the mouth of the original gland.

Retention cysts of the appendix are not very uncommon and many cases have been reported during the past few years by various writers, but after a careful search of the literature I have been able to find no instance of a retention cyst of the cecum exactly similar to the one I am reporting. Harrington Sainsbury,[1] reports the case of a cystic tumor of the cecum met with in a girl of 11 years who died from an attack of typhoid fever. At the post mortem a large, soft, fluctuating tumor, about the size of a duck's egg, was found occupying the cecum and distending slightly the gut. It arose from the anterior wall just above the level of the entry of the ileum. On opening the tumor it was found to be a cyst filled with dark, ropy, mucoid fluid. Under the microscope the outer layer was seen to be mucous membrane similar to that lining the large intestine. The inner layer was much thinned and appeared to resemble a serous membrane, but the writer qualifies this in a foot-note by adding that the epithelial lining of such a cyst was probably mucous in character, but would be much modified by the distention and its appearance still further altered by death. In all probability, he says, it was a retention cyst and further adds that he knew of no similar case, and those whom he consulted were unable to give any reference to cases of like nature.

A. Krogius[2] reports a case of an intestinal cyst in a child 2 months of age, giving rise to obstruction and intussusception. The abdomen was opened and a resection of the gut with formation of an artificial anus was made. Death took place from hemorrhage. The cyst, which had the character of a retention cyst, was of the size of a pigeon's egg and was situated in the ileum close to the valve.

In his paper, Krogius refers to four previous cases, in which a cyst in the intestinal wall encroached on the lumen of the gut and produced symptoms of obstruction.

1. Sainsbury, Harrington: Trans. Path. Soc., London, 1887, xxxviii, 146.
2. Krogius, A.: Ztschr. f. klin. Med., 1903, xlix, 53.

The first case which he quotes was observed by E. Fraenkel[3] in 1851. An infant, a few days old, developed suddenly symptoms of obstruction of the bowels and died. The autopsy revealed as the cause of the obstruction a cyst 2.5 cm. in diameter close to the ileocecal valve; this appears to have had the characters of a retention cyst.

The second case was noted by Kulenkampff[4] in a 3-year-old boy, in whom, suddenly after a dose of calomel, given for obscure symptoms of

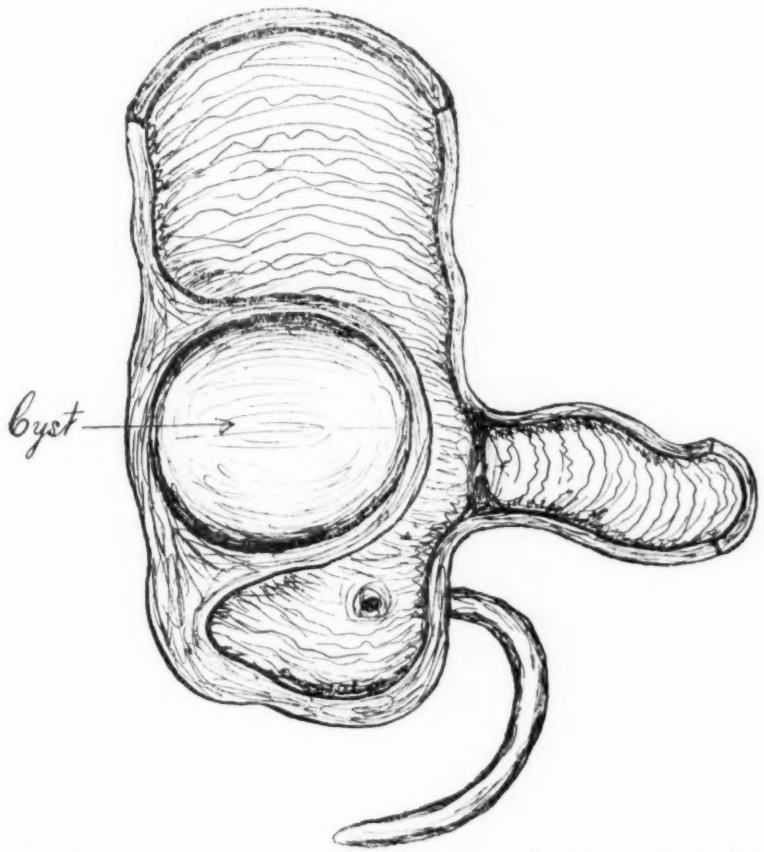

Fig. 1.—Diagram to represent cecum, ileum and cyst cut longitudinally.

obstruction, violent vomiting set in followed by collapse and death. A cyst in the mesentery compressing the ileum appeared to be the cause of obstruction.

The third case was one of obstruction in adult, 62 years of age, due to a cyst which appears to have been of a sarcomatous character.

3. Fraenkel, E.: Virchow's Arch. f. path. Anat., 1882, lxxxvii, 275.
4. Kulenkampff: Centralbl. f. Chir., 1883, p. 679.

The fourth case, reported by Sprengel,[5] occurred in a girl, 15 years of age, who had had occasional symptoms of temporary obstruction since she was 4 years old. Operation became necessary and revealed a cyst apparently lying between the muscular layers of the intestine, and the apparent cause of an ileocecal invagination. The origin of the cyst was uncertain.

Krogius considers his case to be the fifth reported in which a congenital cyst in the intestinal wall was found to be the cause of occlusion of the bowel.

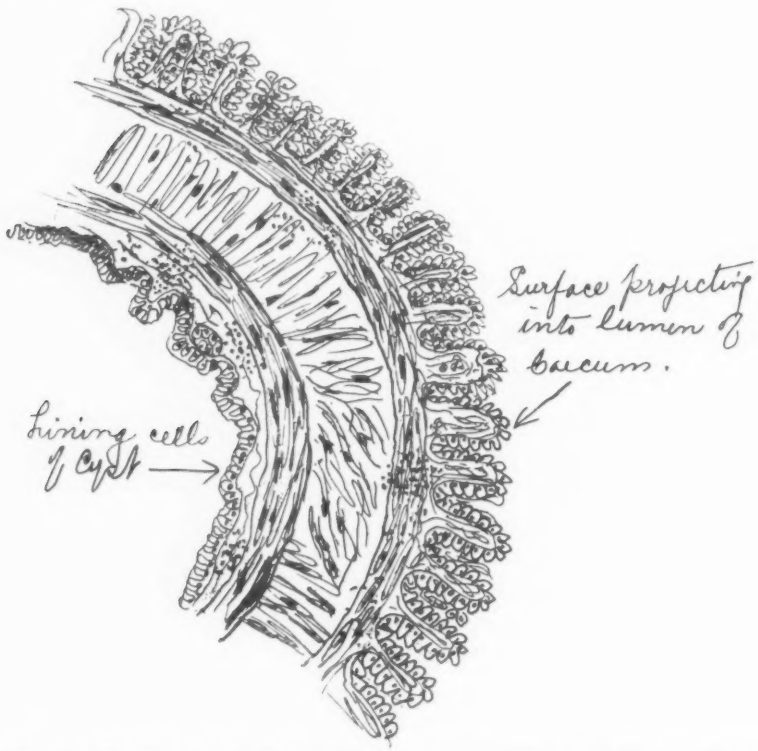

Fig. 2.—Drawing made from section through cyst, showing the internal layer of somewhat flattened epithelium, the three muscular layers, the external mucosa, and the infiltration.

After an extensive search through literature the three cases quoted are the only ones I can find reported of retention cysts in the neighborhood of the ileocecal valve leading to obstruction and invagination.

The following cases have an associated interest, as the clinical symptoms were similar, although the pathological condition had a different origin.

5. Sprengel: Arch. f. klin. Chir., 1900, lxi, 1032.

Chas. A. Morton[6] reports a cyst in the interior of the cecum connected with the base of the appendix, obstructing the lumen of the appendix leading to a cystic dilation of it also. It does not appear, however, to have been a retention cyst for the mucous membrane of the cecum was said to terminate in a ridge around its base. The cyst projected into the lumen of the gut about 1½ inches and was full of amber-colored jelly. Its interior is said to have been smooth, and microscopic examination revealed no mucous membrane covering it or lining its cavity.

Neupert,[7] at the meeting of the Berlin Surgical Society, July 14, 1910, reports the case of a boy 10 years old, admitted to the hospital with a painful circumscribed swelling in the ileocecal region. On opening the abdomen a tumor about the size of a hen's egg was found in the ileum 10 cm. from the ileocecal valve. The tumor occupied the opposite side of the bowel to the mesentery, narrowing the lumen of the bowel. Its surface was smooth and its consistence tense and elastic. Numerous swollen glands were found in the corresponding mesentery. Resection of the gut was performed. The tumor was found to contain sterile pus. Sections of the wall examined microscopically showed a layer of cubical epithelium with traces of a submucosa; tubular glands were absent. Externally and internally the cyst was enclosed by the muscular layer of the intestinal wall. It was therefore regarded as a suppurating cyst, evidently of congenital origin and probably connected developmentally with the omphalo-mesenteric duct.

6. Morton, Chas. A.: Bristol Medico-Chirurg. Jour., 1887, xv, 319.
7. Neupert: Zentralbl. f. Chir., 1910, p. 714.

CARDIAC DISEASE IN CHILDHOOD, WITH SPECIAL REFERENCE TO PROGNOSIS*

CHARLES HUNTER DUNN, M.D.
BOSTON

In 1906 I reported the results of an investigation of certain clinical aspects of rheumatic fever in childhood, which was based on a series of 300 consecutive patients admitted to the wards of the Children's Hospital. Of these 300 patients, 209 were discharged from the hospital with signs of organic valvular disease of the heart. The after history of these cases appeared to me to be a point of great interest, with a practical value bearing directly on the question of prognosis, and on certain aspects of treatment. I determined at the time to keep in communication as far as possible, with all of these discharged patients, and at the same time the scope of the investigation was extended beyond the limit of cardiac disease of rheumatic origin, by including all other patients of cardiac disease admitted to the hospital during the period from which the original series was taken. Cases of patients who subsequently died from intercurrent infection were thrown out.

One of the features of greatest interest in such an investigation is the amount of disability carried into adult life, or at least young adult life, by these patients. It was therefore necessary to follow the after-history of these patients for a period sufficiently long to afford evidence on this point. The period in which the cardiac patients of this series were admitted to the hospital was that of a number of years previous to the summer of 1903. I resolved to follow the cases discharged from the hospital until all of them should have entered at least young adult life, taking the age of 14 years as the termination of childhood. All of these patients have now passed this limit, the youngest survivor having reached the age of 15 years.

ETIOLOGY

The series of cases included in this investigation numbers 304 cases of cardiac disease. It throws a certain amount of light on the relative frequency of occurrence of the various etiologic factors.

TABLE 1.—ETIOLOGY IN CARDIAC DISEASE

	Cases.	Per Cent.
Rheumatic fever	264	87
Congenital lesions	21	7
Some recognized infection other than rheumatic fever	9	3
Unknown etiology	10	3

* Submitted for publication May, 1913.

In compiling this table, in the absence of any laboratory or bacteriologic proof of the existence of rheumatic fever as a specific disease entity, the following clinical evidence of the rheumatic origin of the lesions was employed. All cases which had either during the attack in the hospital, or in previous, or in subsequent attacks, shown symptoms of arthritis or of chorea were classified as manifestations of rheumatic fever. In addition, certain cases of acute endocarditis and pericarditis with fever, in which the clinical picture was precisely similar to other cases in which arthritis did occur, and in which there was no evidence of any other form of infection, were also included. On this basis of classification, no case of acute febrile cardiac disease fell under the heading of unknown etiology, every such case being either due to rheumatic fever, or to some other recognized infection. The cases of unknown etiology were all cases of chronic endocarditis.

The table shows the overwhelming preponderance of rheumatic fever as a cause of cardiac disease.

THE CARDIAC CASES DUE TO RHEUMATIC FEVER

Acute and Chronic Cases.—Patients entering a hospital with cardiac disease, are admitted either on account of symptoms connected with the disease from which they are suffering, or the cardiac lesion is discovered accidentally in connection with the investigation of their illness. In the 264 rheumatic cases, all patients were admitted because of symptoms of this disease, either arthritic or cardiac. Arthritic symptoms in rheumatic fever, under the present most generally accepted theories of the etiology of this disease, may always be regarded as evidence of the existence at the time, of an active infection. Cardiac symptoms, on the other hand, may occur from two causes. They may be due to the existence at the time of an active infection localized in the heart, or they may be due to the so-called broken compensation, caused by calling on a damaged heart to perform a work which is too great for its power. All the cases in the series which had, during their stay in the hospital, symptoms of arthritis, or in which the cardiac symptoms were accompanied by the regular febrile course characteristic of an acute infection, are classified as acute infections. Those cases in which the cardiac symptoms were unaccompanied by fever, and in which there was no history of an immediately preceding febrile attack, are classified as chronic endocarditis.

The relative proportions of acute and chronic cases in the series are shown in Table 2.

TABLE 2.—PROPORTION OF ACUTE AND CHRONIC CASES

	Cases.	Per Cent.
Acute Infection	206	78
Chronic endocarditis	58	22

It appears, therefore, that in childhood, the causes which lead a patient to seek hospital treatment, are more often the symptoms produced by the acute infection with rheumatic fever, than those produced by its after-effects on the heart.

Relation of Cardiac Symptoms to Infection.—In my former paper I expressed the view that in childhood, as distinguished from adult life, cardiac symptoms are more often due to an actual present infection localized in the heart, than to the overstraining of a permanently damaged heart. I believe that the converse of this view is also true. In adult life, the development of an acute endocarditis in the course of an attack of rheumatic fever, is usually described as an insidious process, manifesting itself by the development of an endocardial murmur. In childhood the occurrence of an acute endocarditis is usually accompanied by actual symptoms referable to the heart. The set of symptoms called cardiac, such as precordial pain, palpitation, cough, dyspnea, orthopnea and eventually enlarged liver and edema, are in adults almost always attributed to overstrain. In childhood, this train of cardiac symptoms undoubtedly may be due to this cause, but in the majority of cases it is due to the existence of an actual present cardiac infection. Of course the symptoms are due to an inability of the heart properly to perform its work, but the cause of this inability is to be found in a fresh cardiac infection. The incompetence of the heart is not dependent on the actual amount of valvular insufficiency or stenosis present, for it bears little or no relation to the lesion. It is probably due to the acute myocarditis, which is known to be a frequent, if not an almost invariable, accompaniment of acute rheumatic endocarditis. The accompanying tables give evidence of the relation of cardiac symptoms to the presence of an actual infection:

TABLE 3.—CASES ADMITTED FOR CARDIAC SYMPTOMS

	Cases
Acute infection present	100
Acute infection absent	37

This consideration is of interest in reference both to prognosis and treatment, for it is recognized that the cause of death in the majority of these cases is cardiac failure. If the symptoms leading to such failure are most frequently due to infection, or reinfection, and not to overstrain, this fact has an obvious practical bearing.

In any event I wish to deprecate the use of the term broken compensation as applied to the train of cardiac symptoms described under this name when they occur in childhood. Apparently in only a relatively small number of cases is this term, and the theory on which it is based, applicable to the clinical picture as seen in childhood. In the majority of cases, the cause is not overexertion, but fresh infection. The term

cardiac insufficiency is far preferable to broken compensation, as it is equally applicable to both causes.

The Cardiac Lesions.—The relative frequency of occurrence of the various cardiac lesions is of interest in connection with the subsequent history of these cases. The relation of the form of lesion to prognosis is still a more or less unsettled question in the cardiac disease of childhood. The cases, classified on the basis of the lesions shown during their stay in the hospital, were as shown in Table 4. In only two cases was pericarditis found without any evidence of a valvular lesion in addition. The fifty-eight cases of pericarditis are classified both as pericarditis and according to the endocardial lesion present, and fifty-six of them are counted twice.

TABLE 4.—Occurrence of the Various Cardiac Lesions

	Cases
Mitral insufficiency alone	165
Mitral stenosis alone	5
Aortic insufficiency alone	1
Mitral insufficiency and stenosis	79
Mitral and aortic insufficiency	8
Mitral insufficiency and stenosis with aortic insufficiency	4
Pericarditis	58

Liability in Childhood to Recurrent Attacks of Rheumatic Fever.—The liability in any child attacked by rheumatic fever to recurrent attacks is probably the most important factor in all considerations of the prognosis of the disease. In my first paper the liability to recurrence could only be judged on the basis of the history of attacks of rheumatic fever previous to the one under treatment in the hospital. At present, additional evidence is available, from the following of the subsequent history of the patients throughout the remainder of their childhood, and into adult life, through a period of at least nine and one-half years.

TABLE 5.—Showing Proportion of Recurrences

	Cases
Died in the first attack	17
Recovered without recurrence	47
Recurrent attacks	200

It will be seen that more than one attack of the rheumatic fever infection occurred in 76 per cent. of the cases. Only 17 per cent. showed no recurrence, as in the remaining 7 per cent. no conclusions could be drawn.

Mortality.—The complete investigation of this series of cases seems to me to be of considerable value in connection with the question of the mortality in children with hearts attacked by the rheumatic fever infection. The mortality of the cases in the hospital affords a basis for estimating the liability to death in any one attack of the disease. This is shown in Table 6.

TABLE 6.—IMMEDIATE MORTALITY OF RHEUMATIC CARDIAC DISEASE

	Cases
Died in hospital	55
Discharged, relieved	209

This gives an immediate mortality of 20 per cent. The immediate mortality apparently varies with the character of the process present, as shown in Table 7.

TABLE 7.—IMMEDIATE MORTALITY IN RELATION TO THE CARDIAC LESION

Acute endocarditis	27 out of 148 cases	or 12 per cent.
Acute pericarditis*	18 out of 58 cases	or 31 per cent.
Chronic endocarditis	10 out of 58 cases	or 17 per cent.

* In all but two of these cases acute endocarditis was probably also present.

Table 7 also shows how much more frequently death occurs as a result of an acute infection with rheumatic fever, than as a result of the overstraining of a chronically damaged heart. In forty-five of the fifty-five fatal cases the patient died in the course of an attack of acute infection, so that the mortality from this cause is 82 per cent. of the total.

The subsequent mortality of the cases in this series represents the chances against a child who has recovered from the attack of rheumatic fever in which he is first seen, but who is left with an organic cardiac lesion. The figures are shown in Table 8.

TABLE 8.—SUBSEQUENT MORTALITY OF RHEUMATIC CARDIAC CASES DISCHARGED FROM THE HOSPITAL

	Cases
Lost to view	29
Alive	88
Dead	92

This gives a subsequent mortality of at least 23 per cent. of all cases, and if, as is fairer, the cases lost to view are thrown out, the mortality of these cases is 51 per cent.

The final mortality is that of all cases whether death occurred in the original investigation or after the discharge of the patient from the hospital. It represents the general mortality of rheumatic cardiac disease for ten years, and the chances, so to speak, in the next ten years, against any child attacked by rheumatic fever with cardiac involvement. It is shown in Table 9.

TABLE 9.—FINAL MORTALITY OF RHEUMATIC CARDIAC DISEASE

Died	147
Lived	88

This gives the final mortality as 63 per cent. This of course represents, not the mortality of rheumatic fever, but only of the cases of rheumatic fever in which the heart is affected. During the period from which the figures of this paper were taken, only 17 patients with rheu-

matic fever were discharged from the hospital without evidence of a cardiac lesion. Of these 17 patients, 5 remained well, 5 were lost to view, and 7 had recurrence of acute infection with cardiac involvement. Of these latter, 3 died. Including the 12 cases of rheumatic fever which could be followed, the final mortality of rheumatic fever in childhood is 60 per cent.

Relation of Mortality to Age and to Acute Infection.—This relation is one of the most interesting results of the present investigation. The basis on which the conclusions are drawn is shown in Table 10.

TABLE 10.—RELATION OF MORTALITY TO AGE AND TO ACUTE INFECTION

	Total	Acute	Chronic
Died before 14 years.....	140	109	31
Died after 14 years.....	7	1	6

In this table the cases placed under acute are those in which the patient died in an acute febrile attack, while those placed under chronic died from cardiac failure apparently following the weakening of the heart from overstrain. It appears from the table that a great majority of the patients died as the result of an attack of rheumatic fever, and not as a result of chronic endocarditis. Even among the ninety-two patients who died after their discharge from the hospital, the majority, sixty-five, died in, or shortly after, an acute febrile attack. Such an attack was the cause of the cardiac symptoms producing death. Therefore not only the figures showing the immediate, but also those showing the final, mortality of rheumatic cardiac disease, point to infection as the chief cause of death.

But when the age at which death occurred is considered, the results are of still greater interest. The average age of all the patients at the time of the original investigation was 9 years. Therefore, ten years having elapsed since, at least an equal amount of childhood and young adult life has been lived by these patients. As more than ten years have elapsed since the majority of the original records were taken, more years have been spent over than under 14 years. Nevertheless, the table shows that the great majority of the patients in which a fatal ending occurred, died while still in childhood. Of the ninety-five patients who passed their fourteenth year, only seven have died, while 140 patients died in childhood. These results surely suggest that rheumatic fever is a vastly more serious and fatal disease in childhood.

The significance of the particular valvular lesions present during the patients' stay in the hospital in connection with the mortality of rheumatic cardiac disease does not appear to be great. The study of the valvular lesions in the fatal cases is not conclusive, because of the great preponderance of mitral insufficiency. The only result which is at all

suggestive, is that no patient in whom the aortic valve was affected is now alive.

I believe there are three causes of the very great mortality of rheumatic fever in childhood. First, the greater liability of children to be attacked with rheumatic fever; second, the greater liability of children to recurrence; third, the greater liability of children to cardiac involvement. I cannot give figures in support of all these statements, but the facts are well known to most pediatrists. Table 10 shows that only one patient died after 14 years of age as the result of recurrent acute infection, the other six dying from chronic endocarditis. But 109 patients died under 14 years of age as the result of an acute infection.

We can only conclude that the chief danger in children with rheumatic cardiac disease is in childhood. The danger of death even from chronic endocarditis is greater, as thirty-one out of 140 patients died of chronic endocarditis in childhood, whereas six out of ninety-five patients died from this cause in young adult life. The chief cause of the danger during childhood, however, is the liability of children to recurrent attacks, in which an acute infectious process localized in the heart is the cause of the cardiac insufficiency leading to a fatal ending.

The Disability Following Rheumatic Cardiac Disease Acquired in Childhood.—This is a question of the greatest importance. The survival of eighty-eight patients now under observation, all of whom have entered young adult life, gives a basis for conclusion. The amount of disability is shown in Table 11.

TABLE 11.—DISABILITY IN CARDIAC DISEASE ACQUIRED IN CHILDHOOD OBSERVED IN YOUNG ADULT LIFE

	Cases
Disability great	2
Disability slight	9
Disability none	77

The patients with great disability are unable to work or to lead normal lives. Both of them have been in an adult hospital with broken cardiac compensation. Cardiac symptoms are brought on by comparatively slight exertion. The patients with slight disability have dyspnea on exertion, and some have occasional cough and slight edema. None of them has had an attack of severe broken compensation. They are able to work at sedentary occupations. Seventy-seven patients have no disability. Most of them work, and all of them are apparently leading perfectly normal lives, having had no cardiac symptoms since their childhood. My last set of reports contain many references to activity in dancing on the part of the girls, and in basketball and baseball on the part of the boys. One of the latter asked my permission to enter the twenty-five-mile marathon race. All of these eighty-eight patients still

had their cardiac murmurs when I last saw them. The relation of the amount of disability to the particular valvular lesion is shown in Table 12.

TABLE 12.—Relation of Disability to the Valvular Lesion

Great disability	2 patients have mitral insufficiency
Slight disability	8 patients have mitral insufficiency
	1 patient has mitral insufficiency and stenosis
No disability	56 patients have mitral insufficiency
	19 patients have mitral insufficiency and stenosis
	2 patients have mitral stenosis

When the relative occurrence of the various lesions is taken into account, this table shows no relation between the amount of disability and the character of the valvular deformity.

The relation of the amount of disability to the age at which the patient had his first attack of rheumatic fever is shown in Table 13.

TABLE 13.—Relation of Disability to Age of First Rheumatic Attack

Disability	Age in First Attack, Years	Number of Cases
Great	12 and 13	2
Slight	10 to 14	9
None	2 to 6	50
	6 to 10	20
	10 to 14	7

This table shows that all the patients with disability were attacked when past the age of 10 years, whereas in the cases without disability, the majority were first attacked in early childhood. It suggests that the earlier in childhood a cardiac lesion is acquired, the better will be the result as regards the ability to lead a normal adult life.

It seems to me that the general amount of disability seen in rheumatic cardiac disease acquired in childhood is remarkably small. I believe it to be very much less than the disability following rheumatic endocarditis acquired in adult life. Unfortunately, I cannot give figures bearing on this point, as, while rheumatic fever is fairly common in adults, it attacks the joints alone with such greater frequency than in childhood, that cases in which endocarditis develops for the first time in adult life are comparatively rare. I have not had time to accumulate a sufficient number of such cases to afford a basis for comparison. I believe, however, that such a comparison would show a much less disability in cardiac disease acquired in childhood. My recollection of my work in an adult out-patient department, and in a general hospital, is that the majority of patients suffering from broken compensation or serious disability from chronic endocarditis, could trace the origin of their lesion, if at all, to some attack of rheumatic fever occurring since they had entered adult life. On the other hand, in every adult out-patient department are seen many patients who are seeking medical aid

on account of some affection other than cardiac, in whom, in the course of routine examination, some valvular lesion of the heart is found. In a large number of cases these patients declare that they have never suffered from cardiac symptoms, and have no recollection of any attack of rheumatic fever. I believe that in very many of such patients, the cardiac lesion represents the sequela of an attack of rheumatic fever which occurred in childhood, at an age when the arthritic manifestations are often or so much less pronounced, that they are not remembered. These patients, leading normal lives, yet with every evidence of organic cardiac disease, are common. They correspond to the seventy-seven cases in my series in which no cardiac disability persisted.

A possible explanation of this lessened disability in cardiac disease acquired in childhood, is suggested by the inferences from Table 13. The disability appears to be less, the earlier in childhood the lesion is acquired. In many of the permanent lesions acquired in childhood, the power of adaptation between the damaged organ and the work required of it is greater, and children show a marvelous power of adapting themselves to the requirements of life. In the case of cardiac disease, I believe the so-called compensation of the damaged heart is more than a mere mechanical hypertrophy. I believe that when the lesion occurs during childhood, that is, during the period of active growth, a mutual adaptation between the heart and the child gradually occurs, which is far more perfect than can occur after the period of growth is passed. The child grows up to fit its heart, and the heart develops to fit the child. Only in this way can I explain the facts suggested by this paper. The earlier in life the damage to the heart, the longer is the period of growth during which this adaptation can occur.

Inferences as to the Treatment of Cardiac Disease of Rheumatic Origin.—The outcome of the patients discharged from the hospital is suggestive as regards treatment. Treatment in the chronic endocarditis of childhood resolves itself largely into the question of prophylaxis. If the sole danger to be apprehended were the rupture of compensation by overstrain, prophylaxis would consist simply in the guarding of children with damaged heart valves from overexertion. But we have seen that the chief danger lies in the liability to a recurrent attack of the infection. We know so little of the exact nature of the infecting organism in rheumatic fever, and of its channels of invasion, that we can accomplish comparatively little in preventing recurrent attacks, beside the most general hygiene measures. The evidence in favor of the tonsil as a frequent route of invasion is so great, that, in view of the fatality of the disease, I believe we are justified in advocating the removal of the tonsils in every patient who has had one attack. If a patient who, in addition to having had an attack of rheumatic fever, is subject to tonsillitis, removal

of the tonsils is positively indicated. The frequency and severity of rheumatic fever appears to vary somewhat with climate and locality. Whenever it is possible, I believe we should lessen the chances of reinfection by removing the patients to a place where rheumatic fever is uncommon.

The most important question is how far we should go in guarding against the breaking down of cardiac compensation by overstrain and overexertion. That children are liable to danger from this cause is a fact, as shown by the thirty-one patients in this series who died from chronic endocarditis while still within the limit of childhood. That we should endeavor to guard against dangerous overstrain goes without question. But it is questionable how far our efforts should reach in limiting the normal activities of the child. We must consider the question of lessening the disability in adult life, when the heart must be able successfully to cope with the strain of a normal active life. If such ability is due to a gradual adaptation between the child and the heart, it is very probable that too much limitation of the activities of childhood will prevent this adaptation from taking place, and will leave the child unfitted to encounter the demands of active adult life.

Most of the parents of the patients in my series were given strict directions as to the guarding of their children from overstrain, and as to the limiting of their activities. Some of them followed these directions, while the majority disregarded them entirely. Singularly enough, of those who obeyed these directions at all, the majority obeyed them with exaggeration, limiting the activities of the children to an extreme degree. The relation of the limitation of activity to the mortality from chronic endocarditis is shown in Table 14.

TABLE 14.—RELATION OF TREATMENT TO MORTALITY

	Carefully Guarded	Normal Activity
Died, 37	13	24
Lived, 88	20	68

The proportion of children who lead a life of normal activity during childhood is greater in those who lived than in those who died. It does not seem from this series at least as if the guarding of children from overexertion had any notable effect on the mortality. Moreover, when the cases are analyzed as to the relation between limitation of activity and subsequent disability, it appears that in general those children did better in whom the normal activities of childhood were not limited at all.

I do not mean that we should let our cardiac patients engage in all normal activities without limit, or without supervision. I simply wish to point out the possibility of going too far toward the other extreme. I believe we should avoid putting our cardiac patients under a glass case,

for even normal activity is preferable to extreme limitation of activity. We should remember the other aspect of the question, that of the gradual adaptation of the child to the damaged heart, which takes place during the previous period of growth. We must do all in our power to favor this process, and this can only be done by allowing the heart to accustom itself to increasing demands on its power during this period. Nothing can be more important than the proper management of these cases, for I believe that the future of the child is largely dependent on it. The most thorough supervision is essential. Beginning at an early period after the disappearance of symptoms, with passive motion against increasing resistance, we should constantly increase the amount of activity allowed, by regulated exercises, so long as we can keep within the danger limit, of which the warning signs are extreme rapidity of cardiac action, or slight dyspnea. But we should not stop when a moderate amount of activity can be indulged in without symptoms. We should continue to increase the amount of activity allowed, and if finally these children can indulge in all the activities of childhood without symptoms, I believe we should not hesitate to remove all limitations. Their chief danger during childhood lies in reinfection, not in overexertion, and the more they learn to do in childhood, the better are their prospects for a normal, active, useful adult life.

CONGENITAL CARDIAC DISEASE

The cases of congenital cardiac disease in this series are too few to permit the drawing of conclusions of any great value. There were twenty-one cases.

Open Ductus Arteriosus.—Fifteen cases were diagnosed as open ductus arteriosus. The patients had a murmur, but no enlargement of the cardiac dulness. Two of them had slight cyanosis but no thrill, and two had a palpable thrill but no cyanosis.

The final result in these cases was as follows: Two died, four were lost sight of and nine recovered. The two patients who died, were those having slight cyanosis, and who died in infancy. In one the diagnosis was confirmed at autopsy. Both of the cases in which there was a palpable thrill recovered, with disappearance of the thrill. In all of the nine cases of recovery, and in two of the patients lost sight of, the murmur eventually disappeared, but I am unable to state the exact time of its disappearance. The nine patients are now apparently well, and are between 10 and 16 years of age.

Pulmonary Stenosis.—Five cases were diagnosed as pulmonary stenosis. The patients had a murmur, cyanosis, palpable systolic thrill and enlargement of the area of cardiac dulness. Of these cases, four patients died before they were 2 years old, and one recovered. This patient is still very cyanotic, with the same signs and clubbed finger tips.

Deficient Ventricular Septum.—In one case this diagnosis was made. There was a murmur, enlargement of the cardiac dulness, no cyanosis and no thrill. This patient, seen at 8 months, lived a year, and was then lost sight of.

It would seem that open ductus arteriosus is a comparatively favorable lesion. The most interesting feature is the disappearance of the murmur in the patients who recovered. As open ductus arteriosus is due to a failure of the closing of the ductus by normal obliterating endarteritis, I believe the disappearance of the murmur suggests that the closure is simply delayed, and may normally occur later. In these cases, without thrill, cyanosis, or enlargement, I believe that as far as the cardiac lesion is concerned, a most favorable prognosis should be given.

ENDOCARDITIS OF OTHER ORIGIN THAN RHEUMATIC FEVER

Beside the congenital cases, there were only nineteen cases of endocarditis in the series which could not be connected with the rheumatic fever infection. Of these, ten cases were of unknown origin. Rheumatic fever could not be excluded, but no connection with this infection was found either in their past or subsequent history. Of these cases, four patients were lost sight of, three entered adult life with signs of mitral insufficiency, but no disability, and in the remaining three the murmur disappeared and they are well.

Of the nine remaining patients, two were fatal cases of purulent pericarditis following pneumonia, and two were fatal cases of malignant endocarditis following an alveolar abscess and mastoiditis, respectively. In the other five cases the cardiac lesion was attributed to scarlet fever. Two of the patients were lost sight of and three have no disability. In one of these the murmur has disappeared.

CONCLUSIONS

1. Rheumatic fever is very much the commonest cause of cardiac disease in childhood.

2. Cases with acute rheumatic infection localized in the heart are much commoner than cases suffering from chronic endocarditis.

3. Cardiac symptoms are due to two causes: first, acute infection localized in the heart; second, broken cardiac compensation. Of these two causes the first is the commoner.

4. The liability of children to recurrent attacks of acute rheumatic infection, in any of which the heart may be involved, is very great.

5. The immediate mortality of rheumatic cardiac disease is about 20 per cent.

6. The subsequent mortality of patients with endocarditis of rheumatic origin, followed for at least ten years in about 50 per cent.

7. The final mortality of rheumatic fever followed for at least ten years is 60 per cent.

8. The mortality is seen chiefly during childhood. The mortality after young adult life is reached falls to only 7 per cent.

9. The cause of death is heart failure. The cause of the heart failure may be either acute cardiac infection or broken compensation. In childhood the former cause is far the more common. After adult life is reached the latter cause is more common.

10. The particular valvular lesion present has little or no relation either to the mortality or the amount of disability in adult life; except that aortic disease appears to be a particularly fatal lesion in childhood.

11. The causes of the great mortality of rheumatic fever in children are, first, their greater liability to this infection; second, their greater liability to recurrent attacks; third, their greater liability to cardiac involvement.

12. Patients who escape the dangers of childhood, and who enter adult life, are apt to show a remarkable freedom from disability. The majority of such patients can lead normal active lives.

13. The probable cause of this freedom from disability lies in the fact that the cardiac damage occurs during the period of growth, and during this period a particularly perfect adaptation can take place between the heart and the patient, which enables the heart to meet the demands made on it. This adaptation is more perfect than can be attained in the adult.

14. The earlier in life the cardiac lesion is acquired, the better is apt to be the result in adult life, as concerns ability to lead an active, normal existence; provided that the patient escapes the dangers of childhood.

15. Treatment should be directed toward favoring the adaptation of child and heart. While guarding against overstrain, we must avoid too great limiting of the normal activities of childhood.

16. In congenital cardiac disease, open ductus arteriosus is a favorable lesion.

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THE DIAGNOSIS AND TREATMENT OF PYELITIS IN INFANCY *

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The pyelitis of infancy, which is a fairly common disease, is generally understood by pediatricians, as expressed in their writings, as a disease characterized by an active, remitting temperature, and which is treated most successfully by the use of alkalies, while some cases may be cured by hexamethylenamin in doses of ½ to 2 grains three times a day, or every three hours.

Recent experiences have led me to believe that such statements should be materially modified. We should rather say that the pyelitis of infancy is a disease which is usually characterized by a high remitting temperature, but may give rise to no temperature, and that while some patients may be cured safely by neutralization of the urine with alkalies and others by doses of hexamethylenamin such as those named, that the most efficient treatment in difficult cases is by the use of very large doses of hexamethylenamin aided by vaccines, either commercial or autogenous. In confirmation of this statement I wish to present briefly three cases of pyelitis which I have recently had under observation.

CASE REPORTS

CASE 1.—A healthy female child, 1 year old. One month after a vaccination, which took well, and when it was practically healed the child suddenly had a temperature of 104 F. and examination of the urine showed a pyelitis. Alkaline treatment was prescribed and in four days the urine had cleared and the child had a normal temperature. Nine days later, however, the temperature again arose and the alkaline treatment was prescribed, but after three days, the temperature having gradually risen to 105.6 F., the alkaline treatment was stopped and hexamethylenamin was given in doses of 1 grain every four hours. (Chart 1.) This was changed two days later to 1 grain every three hours and again in two days to 1 grain every two hours, and finally to 1 grain every hour, without any evident effect on the symptoms. The hexamethylenamin was then stopped, it being considered unsafe to continue this dose for many days. Potassium citrate in doses of 5 grains every three hours was again ordered and it neutralized the urine, but under this treatment the temperature began to rise again. At this time a blood examination showed 22,000 white corpuscles, 56 per cent. polynuclears, 3,800,000 red cells and no malarial organisms. The urine drawn by a catheter showed colon bacilli as well as a few colonies of streptococci. Thirty millions of commercial colon vaccines were then administered. Administration of the vaccine was followed in two days by a normal temperature, which, however, quickly reacted up, on the fourth day having reached nearly 102 F., so

*Submitted for publication May 15, 1913.

that on the fifth day a second dose of 50,000,000 colon vaccines was administered, followed immediately by a normal temperature.

The child was then put on benzoate sodium with hexamethylenamin, 12 grains of each during the day. The following day this was increased to 15 grains and the day after to 24 grains. On this day, however, the temperature again arose to 101.5 F. On the twentieth day of the disease the child's weight was 21¼ pounds, showing a gain of 2¼ pounds during the preceding four weeks. The child began to gain weight as soon as the temperature was reduced by the vaccines. The following day, the temperature having risen to 101.4 F., 40,000,000 bacteria were again administered with a prompt reduction in the temperature. The urine continued to show many leukocytes and bacteria. Twenty-four grains of hexamethylenamin daily was continued until the twenty-seventh day of the disease when the following report on the urine was received from Dr. F. C. Wood: "The only Gram-negative bacillus which was found was not the colon, as it did not ferment sugar. There were ordinary staphylococci in small numbers. The specific gravity was 1.010. It showed no albumin or diacetic acid, but many leukocytes and bacteria."

All medication was now stopped. Six days later, the temperature having again arisen to 102.2 F., 30,000,000 of the same vaccines were administered. No

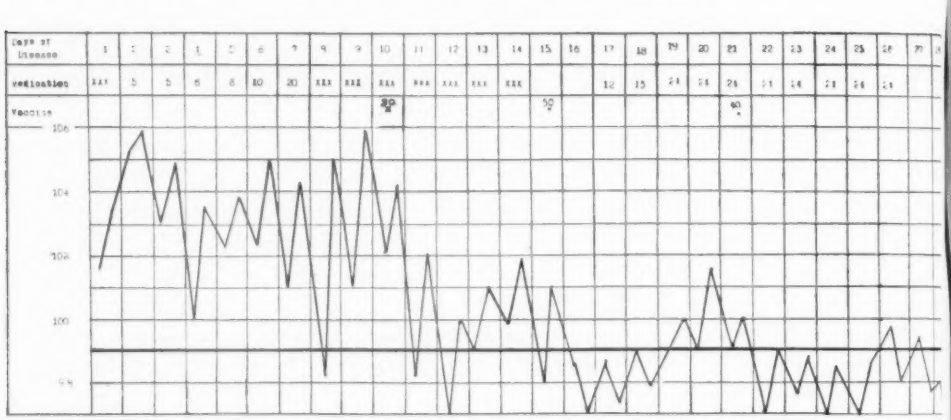


Chart 1.—(Case 1) Temperature curve in an infant with pyelitis. X = millions of vaccine. Arabic

further medication was attempted until the forty-second day when it was decided to try the effect of very large doses of hexamethylenamin for short periods. Twenty-five grains daily without sodium benzoate were then given for four days with a marked diminution in the number of leukocytes and bacteria present. On the fifth day this was run up to 30 grains and on the sixth day to 35 grains, with still a diminution in the bacteria and leukocytes, but without obtaining a sterile urine and without any evidence of irritation of the kidneys. There was no albumin in the urine, and no diacetic acid. On the fifty-fourth day of the disease, after a week without treatment, 40 grains of hexamethylenamin were administered with an improvement in the urinary condition, and on the following day 40 grains and the third day 45 grains, at which time the urine was found to be sterile. Treatment was then stopped and no recurrence of the urinary infection has occurred during the year that has passed.

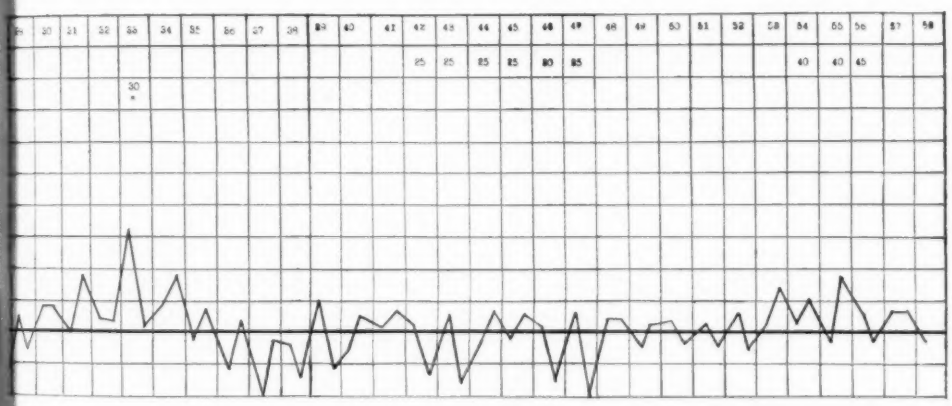
These large doses of hexamethylenamin neither caused any evidence of disturbance of the kidneys nor any interference in the well-being of the child. As soon as the fever was controlled by the vaccines the child

gained in weight and really seemed better when on large doses of hexamethylenamin than at any other time.

CASE 2.—It is interesting to note the long period of lack of fever and constitutional symptoms, but with a continuation of the pyelitis as evidenced by pus and bacteria in the urine after the administration of vaccines, especially in connection with the next case of which I wish to speak in which a similar infection of the urinary tract with colon bacilli occurred in a child 9 months old, who seemed apparently well at the time the urinary infection was found. This child had been under my care since birth and had never had a febrile disturbance.

Dec. 21, 1912, I found that the urine of this apparently healthy child was moderately acid, had a specific gravity of 1.015, contained a faint trace of albumin, a moderate amount of acetone, a faint trace of phenol, clumps of pus and many bacteria, some in chains. The child was put on potassium citrate, 5 grains every three hours. A specimen taken by catheter showed a pure culture of colon bacilli.

After five days of this alkaline treatment, there being no improvement in the condition of the urine, ½ grain of hexamethylenamin was ordered to be given every three hours, so that the child got three grains that day, on the twenty-



Arabic numerals = grains of hexamethylenamin. Roman numerals = grains of citrate of potash.

seventh 5 grains, on the twenty-eighth 10 grains, on the twenty-ninth 12 grains, on the thirtieth 15 grains, and 18 grains on the thirty-first. During this time the urine continued to contain leukocytes and bacteria, the leukocytes varying in number from 12 to 50 in a D field. On January 1, 20 grains of hexamethylenamin were administered, on the second 25 grains, and on the third 30 grains. This dose was continued until the sixth of January, when the urine still continued to be contaminated. The hexamethylenamin was stopped and potassium citrate was again administered. The contamination of the urine continued under this treatment, although several times the urine appeared almost free from contamination, and on this account the alkaline treatment was continued longer than it otherwise would have been. On January 27 four doses of 7 grain each, or 28 grains of hexamethylenamin were given, and on the twenty-eighth 35 grains, on the twenty-ninth 35 grains. On the thirtieth macules appeared on the body, especially adjacent to the upper part of the diaper, and the child had a temperature of 101 F. the night before. She was not taking her bottles very well and had lost ½ pound in four days and the hexamethylenamin was stopped.

With these large doses of hexamethylenamin the urine rapidly cleared and the day after it was stopped a specimen of urine was found to be sterile and no contamination of the urine has since occurred.

This case, then, of colon pyelitis without temperature in an 18-pound baby was cured by 35 grains of hexamethylenamin a day for three days without any evidence of irritation of the kidney or marked interference of the general health. Whether the macules on the body, the loss of half a pound in weight, and the slight rise in temperature were due to the hexamethylenamin I am unable to say.

No vaccines were used in this case as vaccines appear to control the constitutional symptoms and to have little or no control over the inflammation.

CASE 3.—A third case was recently seen by me in consultation with Dr. Thomas F. Lancer. A female child, 6 months old, had been sick six days. On the day preceding the one when I saw the child the temperature had reached 106 (Chart 2). There was a pause at the end of inspiration and an expiratory grunt, and the movements from the bowels contained some mucus.

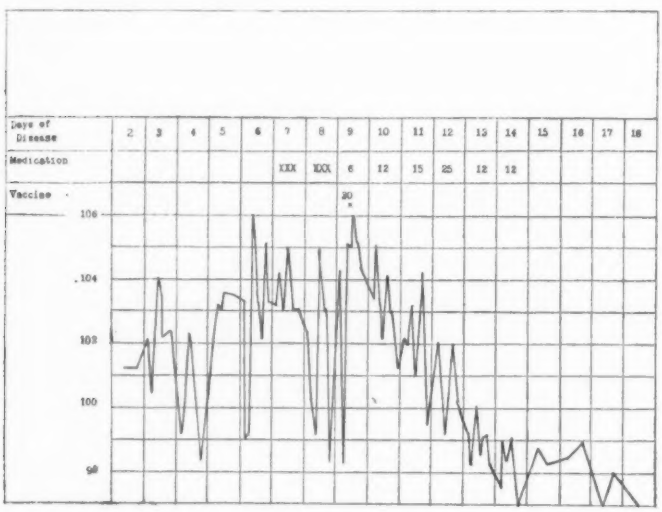


Chart 2.—(Case 3) Temperature curve in an infant with pyelitis. X = millions of vaccine. Arabic numerals = grains of hexamethylenamin. Roman numerals = grains of citrate of potash.

By a system of exclusion a probable diagnosis of pyelitis was made, and the child was put on potassium citrate. An examination of the urine showed a colon pyelitis. After three days on potassium citrate, although the temperature had been lower, the child looked much worse and the temperature arose again to 106 F. Thirty million colon bacilli were then administered and 6 grains of hexamethylenamin were given on this day. No immediate marked decline in temperature followed the administration of vaccines. The following day 12 grains of hexamethylenamin were given, on the eleventh day 15 grains, on the twelfth day 25 grains, and on the thirteenth day the temperature was normal and the urine was sterile.

No disturbance of the child's health was caused by the large doses of hexamethylenamin, 25 grains a day in a 6-months' baby. The urine never contained more than a faint trace of albumin.

CONCLUSIONS

Pyelitis in infancy, due to the invasion of the pelvis of the kidney with colon bacteria resulting in a purulent inflammation, can apparently occur with no perceptible rise of temperature at any time. These cases should be treated and cured by the means ordinarily used in pyelitis.

The alkaline treatment of pyelitis, while it is safe and will control many cases, is markedly less efficient than other methods of treatment.

Vaccines, either autogenous or commercial, are useful in controlling the constitutional symptoms of pyelitis.

Hexamethylenamin, while sometimes effective in doses of from ½ to 2 grains several times a day, will not in these doses cure certain cases which may be controlled by very large doses.

Hexamethylenamin should always be administered in small doses first, but the dose should be rapidly run up, the child and its urine being carefully watched for symptoms of irritation of the kidneys.

Large doses of hexamethylenamin should not usually be continued for more than a week at a time, and then after several days without any treatment or with alkaline treatment it should be started at the maximum dose given before and the amount increased daily until an influence on the urine is obtained. Doses of 25 grains daily in a child of 6 months, and from 35 to 45 grains a day in a child from 9 to 12 months may be safely given in this way to some infants.

211 West Fifty-seventh Street.

ANALYSIS OF ONE THOUSAND CASES OF EPIDEMIC MEASLES *

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Measles may be said to be nearly endemic in communities of children by reason of the regularity of its appearance at certain seasons of the year, and its peculiar partiality for definite age periods. Amongst the diseases of childhood it is conspicuous at times for its great mortality where associated with conditions of poverty and overcrowding. The small, spasmodic outbreaks which occur amongst an urban population may be said to be cyclical, and depending on the arrival of a number of children at the susceptible age period. These localized epidemics are not in themselves of importance from the point of severity or complication; the attack is generally mild and the healthy child does not suffer from complications or resulting ill effects. The seasonal outbreak of measles of a low type of virulence is a different disease from that witnessed at times in the fulminating epidemics. In these the manifestation is of a wide and rapidly spreading nature, and its potentialities for immediate and remote physical mischief to the child, are much increased. The infecting agent seems to become aggravated as the cases increase in number, complications become constant and severe, instead of occasional and mild, and the tendency to serious sequelae is much enhanced. The mortality at these times is sometimes very high, particularly in institutions for children (15 to 35 per cent., Holt); on the other hand, a lower rate pertains in homes where the necessity for keeping a number of children of susceptible age in close association does not exist (4 to 6 per cent., Holt).

During the years 1910 and 1911 outbreaks of measles of an exceptional nature occurred amongst the emigrant children arriving in the port of New York. It was believed that an account of these cases would be of interest as possessing certain unusual features of their own, as well as from the large number under observation at the Hoffman Island Isolation Hospital during that period.

For the proper appreciation of the factors underlying the occurrence among a certain class of an epidemic disease of exceptional severity, there should be first considered the physical condition of the individual, including also the nature of his environment, before and at the time of attack; the number of cases among a susceptible community and the

* Submitted for publication April 25, 1913.

severity of the symptoms move in a kind of arithmetical progression with the sum of the conditions that produce ill health. That this is a truism is well borne out by experiences of war and disaster. In the great stream of emigration that sets in toward the United States at certain seasons of the year, the emigrant child is borne along, always a helpless victim of the flow of world populations. If we inquire into the circumstances of this child emigration we will find that after being taken from the home village, the discomforts of a long railway journey (at minimum rates) constitute only the beginning of a long period of hardship before sailing. Frequently there is a detention in observation camps for many weeks, in an environment far from resembling the home life, and a certain exposure to every form of infectious disease.

Although the law requires that none but healthy children of emigrants be allowed to embark with their parents, even the healthiest children cannot readily adapt themselves to the changed conditions of life on board ships. To meet this new experience, the emigrant child after weeks of privation has little or no store of resistance to draw on for any emergency. The proper amount of fresh air and exercise, so necessary to young people who have lived in the open, cannot always be obtained in stormy weather at sea, and this is a very frequent occurrence in the North Atlantic during the two or more weeks voyage from the Mediterranean ports. The parents themselves are often so prostrated with seasickness that they are unable to care properly for the children. The unavoidable crowding in confined spaces and the concurrent weakness resulting from seasickness all tend to render the emigrant child particularly susceptible to infectious disease. It is among material of this nature that quarantine experience shows the epidemic disease of childhood assumes a gravity little known in communities ashore. The following tables and figures presented here are taken from the records of a thousand cases of epidemic measles occurring among emigrant children treated at Hoffman Island Isolation Hospital during nine months of 1910-1911.

SEASONAL INCIDENCE

Reference to Table 1 will show that most of the cases occurred in December and April, May and June. The annual summer and winter maxima are well accentuated, the number being 186 for June and 145 for December, respectively. Nearly half the total number occurred in the three months April, May and June.

SEX INCIDENCE

The sexes were very evenly balanced, the numbers being 490 male, 510 female.

AGE INCIDENCE

The age incidence of attack varies somewhat from that usually recorded in measles. The greater number appears in the three-year age period, 195 (Tables 3 and 4); the two-year period ranking next with 166, and the under-one-year period third with 140. The number of cases under one year is unusually high. Three years and under contribute 603 cases (60.3 per cent.); over ten years the number is 48; over twenty years, 10.

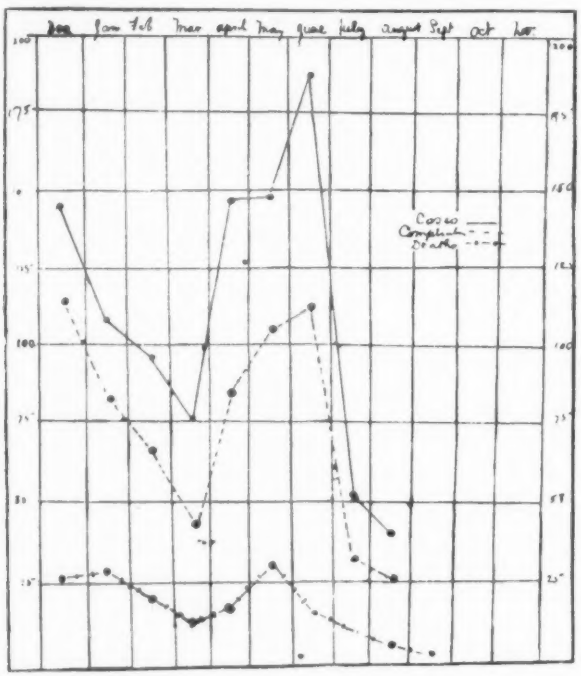

Chart 1.—Monthly curves of cases and incidence of complications and deaths in 1,000 cases of measles.

THE COMPLICATIONS

The index of the severity of a measles outbreak depends on the number and character of the complications, and it is to these alone that the high mortality at times is due. The disease being essentially one whose outward manifestation is a catarrh of the mucous air passages, it is by the various continuation of these into special parts that the complications arise. In this epidemic the outstanding feature was the occurrence of purulent otitis media in 495 cases, of which 353 were affected in both ears. To place the occurrence of the otitis under the various age periods we found that, one year and under, 42.9 per cent. of the cases

TABLE 1.—Number of Cases, Complications and Mortality, Arranged According to Months, in 1,000 Cases of Measles

Month	Cases	Complications	Mortality	Month	Cases	Complications	Mortality
January	107	78	27	July	51	32	10
February	97	68	21	August	44	26	6
March	75	44	12	September	...	..	3
April	147	84	14	November	...	..	..
May	148	105	28	October	...	..	..
June	186	113	18	December	145	114	26

TABLE 2.—Percentage of Complications and Deaths in Each Month

Month	Cases	Percentage of Complications	Percentage of Deaths	Month	Cases	Percentage of Complications	Percentage of Deaths
December	145	78.6	17.9	May	148	70.9	18.9
January	107	72.8	25.2	June	186	60.7	9.6
February	97	70.1	21.6	July	51	62.7	19.9
March	75	58.6	16.0	August	44	59.0	13.0
April	147	57.1	9.5				

The above table shows graphically the number of measles cases in each month with the percentage of complications and fatal cases. Greatest percentage of complications occurred in the four months of December, January, February and May. June with the greatest number of cases had a small complication incidence and the smallest case mortality of all the months but April. The months of January and February show the highest case mortality, 25.2 and 21.6 per cent., respectively.

TABLE 3.—Number of Cases, Complications and Mortality in 1,000 Cases of Measles Arranged According to Age

Age	Cases	Complications	Mortality	Age	Cases	Complications	Mortality
Under 1 year...	140	101	43	6 years	54	33	8
1 year	102	83	36	7 years	42	32	0
2 years	166	111	37	8 years	32	18	1
3 years	195	127	24	9 years	20	9	0
4 years	122	77	10	10 years	9	3	0
5 years	70	42	6	Over 10 years.	48	29	2

TABLE 4.—Percentage of Complications and Deaths at Each Age Period

Age Period	Cases	Percentage of Complications	Percentage of Deaths	Age Period	Cases	Percentage of Complications	Percentage of Deaths
Under 1 year...	140	72.1	30	6 years	54	61.1	14.8
1 year	102	81.3	34.3	7 years	42	76.1	....
2 years	166	66.8	22.2	8 years	32	56.2	3.1
3 years	195	65.1	12.3	9 years	20	45.0	....
4 years	122	63.1	8.1	10 years	9	33.3	....
5 years	70	60.0	8.5	Over 10 years ..	48	60.4	4.1

The above table shows the number of cases occurring in each age period with the percentage of complications and deaths. The one-year period shows the greatest incidence of complication and deaths. The first three age periods show more than twice the number of fatal cases of all the other age periods combined.

TABLE 5.—Causes of Death in Age Periods

Disease	Years											
	Under 1 yr.	1	2	3	4	5	6	7	8	9	10	Over 10	Total
Bronchopneumonia ...	10	3	6	3	3	..	..	..	..	..	..	1	26
Bronchopneumonia and otitis media	1	1	7	4	1	1	2	..	..	..	..	..	17
Bronchopneumonia and diphtheria	9	4	6	2	3	1	3	..	..	..	..	..	28
Bronchopneumonia, diphtheria and otitis media	4	2	4	2	4	..	2	..	..	..	..	..	18
Bronchopneumonia and enteritis	12	19	7	1	..	..	..	..	..	..	..	..	39
Bronchopneumonia and pertussis	2	1	2	1	..	..	..	..	..	..	..	..	6
Bronchopneumonia and cellulitis	..	..	..	..	1	..	..	..	..	..	..	..	1
Lobar pneumonia	..	..	..	1	..	..	..	..	..	..	..	..	1
Empyema	1	1	1	4	1	..	..	..	1	..	..	1	10
Diphtheria and otitis media	..	1	..	1	..	..	..	..	..	..	..	..	2
Disseminated tuberculosis	1	2	..	..	..	1	..	..	..	..	..	..	4
Pyemia	1	..	..	..	..	..	..	..	..	..	..	..	1
Mastoiditis and sepsis	..	..	..	..	..	1	..	..	..	..	..	..	1
Enteritis	3	1	1	..	1	..	..	..	..	..	..	..	6
Noma	..	1	1	..	..	1	..	..	..	..	..	..	3
Tonsillar gangrene and sepsis	..	..	..	..	..	1	1	..	..	..	..	..	2
Peritonitis, acute suppurative	..	..	..	..	..	1	..	..	..	..	..	..	1
Marasmus	1	..	..	..	..	..	..	..	..	..	..	..	1
Totals	45	36	35	19	14	7	8	0	1	0	0	2	167

were affected. Two years 54.2 per cent. Three years 52.89 per cent. Four years 54.0 per cent. Five years 47.1 per cent.

Otitis media as a complication in so large a number of the cases tended to increase the severity of the complications and sequelae of measles, the possibilities of septic infection and of long suppurative processes being much increased under these conditions. The day of onset of the otitis was found to be variable; although the membrana tympani might be found red and congested during the first week, indications of pus were not usually found before the tenth or twelfth day of the disease. This was at times accompanied by a rise in the temperature, but an active suppurative process could proceed with little or no indication in the temperature chart. After paracentesis and irrigation, temperature and clinical symptoms subsided rapidly.

Nearly a quarter of all the cases, 20.4 per cent., developed a bronchopneumonia as a severe and typical complication — 204 cases. Enteritis and ileocolitis were present in 156 cases; this was an especially fatal complication in children of one year and under. Along with bronchopneumonia it accounted for 23.3 per cent. of the total deaths. The deaths from bronchopneumonia and enteritis numbered 39, of which 31 were of one year and under. Cervical adenitis, 78 cases, was frequently associated with a lymphadenitis of the axilla or submaxillary area.

Scarlatina as a complication of measles occurred forty-five times. Where measles occurred as a complication of scarlatina, it was recorded as a plain measles case. Mastoiditis, 47; of these, 42 were operative and 8 were double infections. Capillary bronchitis was present in 17 cases and lobar pneumonia in 11.

Acute nephritis as a late manifestation occurred in 7 instances, usually at the twentieth to the thirtieth day. Although these cases had not been clinically observed as having suffered from a concurrent scarlatina, it could not be altogether excluded as a causative factor.

Three cases of noma and 2 of tonsillar gangrene were recorded, all ending fatally. Vaginitis was present in 50 cases. A number of these were of gonorrheal origin, as shown by positive examination of vaginal swabs. Diphtheria was a frequent complication, especially among the very young children — 143 cases; including diphtheria of the nose alone, 23; throat and nose, 10; eye, 5. Diphtheria with bronchopneumonia and otitis media were responsible for 28.7 per cent. of the total deaths. Measles with hemorrhagic rash, 3 cases with one death. Empyema, following bronchopneumonia or simple pleurisy, 13 cases, with 10 deaths. Pyemia with multiple abscesses, 2 cases, with one death. Purulent conjunctivitis, 16. Abscesses, 32 (including 12 of the scalp). Impetigo, 11.

THE FEVER IN MEASLES

The fever in uncomplicated measles is not high, usually running between 103 and 104 F. The duration of the fever after the apppearance of the rash may be variable and its undue extension dependent on very slight causes in children. In 24 cases observed, the average duration was two days, in 128 cases it was three days, and in 236 cases it was four days. If the temperature remains high after the fourth day, or a continued hyperpyrexia has been present from the beginning, a grave complication is almost certain to supervene.

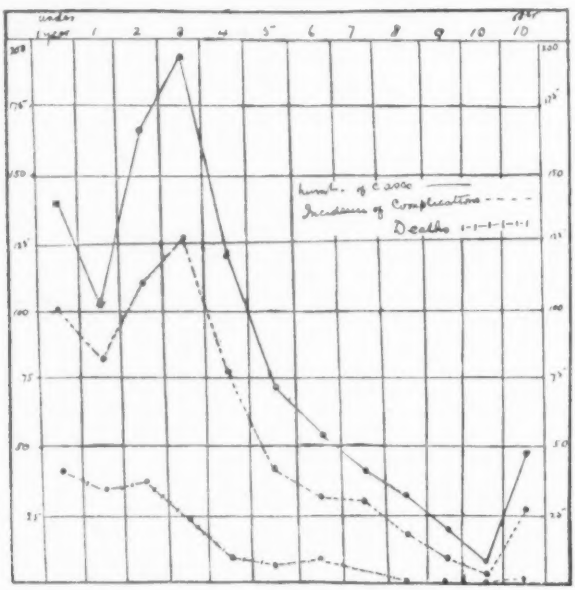

Chart 2.—Age, curves of incidence of cases, complications and mortality.

FATALITY OF HIGH TEMPERATURE IN MEASLES

For the purpose of obtaining some information as to the ratio between temperature and mortality in measles, the following observations were made:

Highest temperature not over	102	F.,	128 cases,	1 death,	mortality 0.78 Pct.
Highest temperature between	102-103	F.,	87 cases,	4 deaths,	mortality 4.5 Pct.
Highest temperature between	103-104	F.,	145 cases,	5 deaths,	mortality 3.4 Pct.
Highest temperature between	104-105	F.,	198 cases,	40 deaths,	mortality 25.2 Pct.
Highest temperature between	105-106	F.,	121 cases,	45 deaths,	mortality 37.2 Pct.
Highest temperature between	106-107	F.,	28 cases,	15 deaths,	mortality 53.5 Pct.
Highest temperature over	107	F.,	1 case,	1 death,	mortality 100 Pct.

From the above it will be seen that the liability to a fatal issue increases directly with the rise in temperature. It is also noteworthy that 46.5 per cent. of the 28 cases with a temperature reaching between

106 an 107 F. recovered. An initial high temperature does not always indicate a severe attack of the disease.

THE INCIDENCE OF COMPLICATIONS

It will be seen by Tables 1 and 2 that the greatest monthly percentage of complications occurs in December and January, showing that in every hundred cases of measles in those months, 78.6 and 72.8 per cent. of them suffered from complications. June, with the greatest number of cases, had a small complication incidence, 60.7 per cent. The incidence of complications for the age periods are shown in Tables 3 and 4. It will be seen that the one-year age period shows the highest percentage of complications, in that every hundred cases of measles at that age had complication in 81.3 per cent. of them.

MORTALITY

The total number of deaths was 167; case mortality 16.7 per cent. The causes of death for the age periods are given in Table 5. By far the greatest number of fatal cases are due to bronchopneumonia in association with some other complication. With enteritis the number is the largest, 39; with diphtheria, 28; bronchopneumonia alone, 26; with otitis media, 17; empyema, 10, and enteritis alone, 6. The greatest case mortality is in the one-year age period, 34.3 per cent. (Table 4). The first three age periods together show more than twice the number of fatal cases of all the other age periods combined. After 3 years the case mortality decreases enormously. Case mortality is nearly equal for both sexes. The greatest monthly case mortality occurs in January, 25.2 per cent., and February, 21.6 per cent. April has the lowest monthly case mortality, 9.5 per cent. (Table 2).

SEQUELAE

Pertussis was the most frequent of the sequelae, 32 cases being recorded. Miliary tuberculosis occurred in four cases, with four deaths. A right-sided hemiplegia of face and eyelid was observed in a female child, aged 1 year, on the thirty-second day of the disease. Recovery took place.

SUMMARY

Of the 1,000 cases of measles the greatest number were in the month of June (186).

The third year age period shows the greatest incidence of attack (195). The largest complication percentage, 81.3, and case mortality, 34.3 per cent., are found in the first year period.

The seasonal prevalence of complication was highest in December, 78.6 per cent., and of case mortality in January, 25.2 per cent.

The most frequent complication was otitis media, 495.

The most common cause of death, bronchopneumonia and enteritis, 23.3 per cent. of total deaths. Average duration of the fever, four days. The onset of purulent otitis media on tenth or twelfth days may not be attended by unusual fever. If the temperature remains high after the fourth day, a possible grave complication is imminent. An initial high temperature does not necessarily point to a possible severe attack.

I am indebted to Dr. S. B. Ragsdale of the Quarantine Staff for assistance in the preparation of the figures on the fatality of high temperature in measles.

PROGRESS IN PEDIATRICS

RÉSUMÉ ON THE CIRCULATORY SYSTEM

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HEART-BLOCK

The incident of heart-block in acute infectious diseases such as diphtheria, typhoid fever, pneumonia, influenza and endocarditis, is recognized, since the use of polygraphic tracings, as being more and more frequent. Sudden death is not infrequently due to lesions of the a-v bundle; and many cases of bradycardia, especially in diphtheria, are unquestionably caused by complete or partial heart-block, and not by vagus inhibition.

Hecht[1] emphasizes the importance, for the rendering of the prognosis, of determining whether the heart-block is due to an organic lesion of the bundle fibers, or to a functional inhibition of their conductivity. He mentions two illustrative cases, one of diphtheria, the other of measles. Atropin caused no change in the disturbance of the stimulus conduction, merely increasing the sinus frequency, in the diphtheria case; while the disturbance in the stimulus conduction disappeared almost entirely, after atropin in the case of measles. The disturbed conduction persisted unchanged during four months in the diphtheria case; whereas in the measles case it was replaced as soon as eight days later by a nearly normal behavior, and after three weeks by entirely normal conditions. In view of its transitory character, and its reaction to atropin, the case of measles block must be designated, clinically, as functional. Robinson and Draper[2] have shown by means of the electrocardiograph that in a man with a normal heart, vagus stimulation will cause not only a marked slowing of both auricles and ventricles, but also a depression of conductivity of the heart beat from auricles to ventricles.

HEART IN DIPHTHERIA

Rohmer[3] studied the heart by means of the electrocardiograph in several cases of diphtheria, to find the relation of anatomical lesions of the atrioventricular bundle to sudden death, and also with the object of investigating whether diphtheritic myocarditis exerts a specific influence

1. Hecht, A. F.: Ztschr. f. Kinderh., 1912, iv, 546.
2. Robinson, G. C., and Draper, G.: Jour. Exper. Med., 1911, xiv, 217.
3. Rohmer, P.: Jahrb. f. Kinderh., 1912, lxxvi, 391.

on the curve of the electrocardiogram, and if so, how far it may be of prognostic value. Two cases presented clinically the undoubted picture of atrioventricular dissociation, which in one instance could also be demonstrated by means of the electrocardiogram. The heart-block in these two cases appeared two or three days before death and persisted unchanged. The almost complete anatomical integrity of the bundle in these two cases proves that it may be poisoned up to a total loss of its function without this intoxication being anatomically demonstrable. Rohmer believes that specific relations to the diphtheria toxin do not exist and that diphtheritic heart death is not due to an elective damage of the His bundle, although the loss of transmission in a severely affected heart must necessarily act injuriously and make prognosis more grave. Myocarditis in the course of diphtheria produces no change in the electrocardiographic picture unless the heart failure reaches a pronounced degree.

Tanaka,[4] in studying serial sections of the heart in fifteen children dying during or soon after an attack of diphtheria, found that fatty degeneration of the heart muscle was the most important change. The amount of degeneration of the atrioventricular bundle showed no relation to that of the rest of the heart; in some cases the bundle of His showed fatty or hyaline degeneration, while the rest of the myocardium was nearly free from it, and vice versa. Neither did sudden paralysis of the heart have any relation to lesions of the bundle of His.

Price and Mackenzie[5] report a case of heart-block in diphtheria associated with auricular fibrillation. This is the first recorded instance of a case of this kind occurring in diphtheria. The heart muscle showed extreme degeneration, but the sino-auricular node and the auriculoventricular node and bundle were not involved. Pepper and Austin[6] have reported a case of complete heart-block in a man 40 years of age, in which there was no demonstrable lesion of the bundle of His, and cite six similar cases previously reported. On the other hand, Cowan, Fleming and Kennedy[7] report two cases of complete heart-block, one diphtheria, the other malignant endocarditis, and three cases of acute endocarditis with nodal rhythm, in all of which the a-v node or bundle was involved in an acute inflammatory process. Butterfield[8] reports a case of heart-block with an acute infection of the whole heart including its membranes. Although the whole heart showed a diffuse inflammatory infiltration it reached its greatest intensity in the auriculoventricular node.

4. Tanaka, T.: Virchows Arch. f. path. Anat., 1912, ccvii, 115.
5. Price, F. W., and Mackenzie, I.: Heart, 1912, iii, 232.
6. Pepper, W., and Austin, J. H.: Am. Jour. Med. Sc., 1912, cxliii, 716.
7. Cowan, J., Fleming, G. B., and Kennedy, A. M.: Lancet, London, 1912, i, 277.
8. Butterfield, H. G.: Heart, 1912, iii, 203.

SYPHILIS

Recent work of Warthin[9] shows that syphilis plays a rôle in the etiology of heart disease, the importance of which has heretofore been unsuspected. In the study of a large number of cases of congenital syphilis, he has found fatty degeneration of the heart muscle present in every case, either as a diffuse fatty change or a focal process. The diffuse fatty change is found in the more severe cases of diffuse interstitial change and is associated with the cellular infiltration, fibroblastic proliferation and myxomatous stroma of this form of syphilitic myocarditis. In lesions of this type, spirochetes are always found in great numbers. The focal fatty areas may occur independently of any infiltration or proliferation, or of any vascular obliteration. With hematoxylin and eosin preparations these areas suggest simply an edema with fatty degeneration of the muscle fibers, but examination by the method of Levaditi shows the presence of spirochetes. Warthin believes that colonies of spirochetes associated with focal fatty changes alone represent either a milder or a more acute infection. In very mild or latent infections colonies of spirochetes have been found in tissues showing no histologic changes at all.

It seems probable that these parenchymatous lesions may heal without an interstitial reaction, as focal fibroid areas and focal calcification of the degenerate muscle fibers have been found in a late stage of congenital syphilis. The important fact that spirochetes may be found in the heart muscle and in no other organ has been demonstrated in two cases of congenital syphilis.[10] The fact that the heart may show marked lesions in cases of congenital syphilis, when the liver, lungs and spleen show no changes at all and no spirochetes, has a great practical importance in pathologic diagnosis.

In seventeen fetuses and new-born infants known to be syphilitic by the presence of spirochetes in the principal organs, Rebandi[11] found in thirteen of these definite histological changes in the aorta. Even under the low power there is seen an increase in the thickness of the aortic wall, which is chiefly confined to the adventitia and media. The vasa vasorum, some of which appear enlarged and hyperemic, others with a sometimes considerably reduced lumen and abnormally thickened walls, are surrounded by a small cellular infiltration. This infiltration varies in intensity in individual cases, involving the adventitia, the outer layers of the media, very rarely the intima. The lesions are similar to those found in syphilitic aortitis in adults. Spirochetes were found in all cases and their number was in direct proportion to the severity of the pathologic changes. No instance was found in which spirochetes were present

9. Warthin, A. S.: Jour. Am. Med. Assn., 1912, lviii, 409.
10. Warthin, A. S., and Snyder, E. J.: Jour. Am. Med. Assn., 1912, lviii, 689.
11. Rebandi, S.: Monatschr. f. Geburtsch. u. Gynäk, 1912, xxxv, 681.

without histologic change, as Warthin has found in the heart muscle. In mesaortitis, the presence of the spirochetes must usually, though not always, be considered as the efficient cause, but in certain cases the agent of the arterial affection is probably simply due to the syphilitic toxins. Panaortitis is always due to the presence of spirochetes.

Levy-Frankel[12] concludes that congenital syphilis is the most common cause of chronic aortitis, and also believes that the pathologic changes may be either microbic or toxic. He states that the adrenal glands, in all probability, play an important part in the pathogenesis of certain atheromatous lesions which at first glance appear to be referable to rheumatism or chorea. Hypertrophy and hyperplasia of the medullary layer of the adrenal glands were noted in two cases, in conformity with the findings of Aubertin and Clunet, who pointed out the frequent co-existence of medullary hyperplasia in the adrenals of adults with atheroma.

ARTERIOSCLEROSIS

Rittenhouse[13] has confirmed Hamburger's[14] observations on arterial rigidity in children. His conclusions are based on the examination of 250 well children between 2 and 14 years. No rigidity was found in twenty children at the age of 2 years. Below the age of 7 years, rigidity of the arteries was exceedingly rare, but was found in 50 per cent. of the cases between the ages of 7 and 10, and in 80 per cent. of the cases at the age of puberty. Rigidity of the temporal arteries was commonest under the age of 6, while the radial arteries were more often affected from the age of 7 onward. With one exception, all the children in whom a high degree of arterial rigidity was detected, showed nervous symptoms. No relation between high blood-pressure and arterial rigidity was observed.

BLOOD-PRESSURE IN INFECTIONS

Rolleston[15] has studied the blood-pressure in diphtheria and scarlet fever and concludes that while sphygmomanometry is of considerable theoretical interest, it is of little practical importance except in the convalescence of scarlet fever when nephritis is a complication. In such a case it may give some indication of the severity of the renal lesion. In only twelve out of thirty-three cases of nephritis, however, was the blood-pressure above normal, and the hypertension never extreme nor of long duration. Findlay[16] found that the older the individual and the higher the blood-pressure, the greater the difference in systolic pressure in the brachial and digital arteries. In childhood and youth the systolic

12. Levy-Frankel, A.: Arch. d. mal. du cœur, 1912, v, 625.
13. Rittenhouse, W.: Wien. klin. Wchnschr., 1912, xxv, 920.
14. Hamburger, F.: München. med. Wchnschr., 1911, lviii, 250.
15. Rolleston, J. D.: Brit. Jour. Child. Dis., 1911, viii, 433; 1912, ix, 444.
16. Findlay, L.: Quart. Jour. Med., 1911, iv, 489.

pressure in the digital arteries equals that registered in the brachial artery. In adults, on the other hand, and in diseases accompanied by high blood-pressure, the systolic brachial pressure is much higher than the systolic digital pressure. Consequently, pressure readings with the Gärtner tonometer, while unreliable in adults, are reliable in children, except in cases of high blood-pressure.

CONGENITAL HEART DISEASE

In studying, by means of the orthodiagraph, the configuration of the heart outline in congenital heart disease, P. and F. M. Groedel[17] have been able to establish certain distinctive radiographic features in the different types of the disease. Defects of the septum may be recognized precisely by the absence of a change in the configuration of the heart outline. A defect in the ventricular septum can be established on the basis of the peculiar ventricular movements of the margin of the right heart shadow, and be distinguished in this way from a patent foramen ovale. The bulging of the pulmonary artery is characteristic of congenital aortic stenosis and persistence of the ductus Botalli. In the case of the latter, the heart appears in mitral configuration (upright); whereas it lies in the form of a cylinder in aortic stenosis. Pulmonary stenosis furnishes no typical shadow. Of all the congenital lesions of the heart a persistent ductus Botalli gives the most typical x-ray picture.

Wessler and Bass,[18] in five cases of persistent ductus Botalli, found the bulging pulmonary artery as described by the Groedels. The heart in pure patent ductus arteriosus shows no enlargement nor alteration in shape. The presence of such changes suggests an associated or complicating lesion. In mitral disease the pulmonary artery may be enlarged, but it does not pulsate as it does in a patent ductus arteriosus. This shows the necessity of making the diagnosis from a fluoroscopic examination.

ARHYTHMIA

Friberger's[19] investigations on arhythmia in healthy children is of unusual interest. These were conducted on 321 unselected school children, between 5 and 14 years of age, and included an examination of the entire body as well as sphygmographic curves. None of these children presented a perfectly regular pulse. A fairly regular pulse was found in 37.4 per cent., a moderately irregular pulse in 50.4 per cent., and a very irregular pulse in 12.2 per cent. The genesis of the arhythmia was uniform, in so far as the direct origin of the irregularity must be referred to a point of the stimulus-producing and stimulus-conducting system, situated above the auricle. Three principal forms of arhythmia were

17. Groedel, P., and F. M.: Deutsch. Arch. f. klin. Med., 1911, ciii, 413.
18. Wessler, H., and Bass, M. H.: Am. Jour. Med. Sc., 1913, cxlv, 543.
19. Friberger, R.: Arch. f. Kinderh., 1912, lviii, 30.

noted: (1) In the majority of cases, long pulse beats alternated with shorter ones in such a way that the duration of the wave is gradually lengthened during a few beats, after which it again becomes gradually shortened; (2) the frequency is suddenly retarded at irregular intervals and then gradually increases again; (3) appearance of disorderly, irregular beats, which are about 0.1 second longer or shorter than their neighbors.

The cases not infrequently presented certain irregularities which agreed in no way with the above-noted principal manifestations of juvenile arhythmias, but rather suggested the idea of extra-systoles, or omitted systoles respectively. In all the curves showing pictures suggestive of extra-systoles, or of sino-auricular block, a distinct respiratory arhythmia was demonstrable, at least for certain distances; this as well as the extra-systoles may possibly have the same genesis. In no case examined was the respiratory type of arhythmia altogether absent, and the establishment of this fact is believed to be not devoid of value for the interpretation of the genesis of juvenile arhythmia.

The higher degrees of arhythmia are usually found in the younger children. Among children 5 to 6 years old, only 14.3 per cent. had a fairly regular pulse; among the 12-year-olds, 58.0 per cent. had such a pulse; among the 14-year-olds, 50.0 per cent. Arhythmia was found to be only slightly more common in girls. Height, weight and muscular development seemed to exert no influence on the frequency of arhythmia. With special reference to the condition of the circulatory organs it is noteworthy that arhythmia occurs more often with abnormally high, or abnormally low pulse rates, than with the rate which is the rule for that particular age. In a selected group of thirty-four children, presumably having weak hearts, arhythmia was about as frequent as in the rest of the material. Among nervous children it was only slightly more common than in others. Among children whose hemoglobin was 70 per cent. or less, 98 per cent. showed arhythmia. In children with habitual symptoms of gastro-enteric disease, arhythmia is not more common than in other children. The pulse of children varies not only in regard to frequency, but also as to volume, although not to a marked degree. The chief result of this investigation consists in the demonstration of the presence of arhythmia in all children between 5 and 14 years of age, so it must be considered as being physiological. Juvenile arhythmia is not a transitory, variable phenomenon, but represents a fairly constant property of the individual in whom it is found. Concerning the causative factors which determine the various degrees of the arhythmia, the findings fail to afford much information. The age is undoubtedly of importance, as is also the condition of the blood. On the other hand, no special influence seems to belong to differences in bodily development, a mild degree of cardiac weakness, or instability of the nervous system.

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